Medication Safety in New Zealand General Practice

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Abstract

Background

General practice has been traditionally considered a low-risk healthcare setting, however high patient volumes and high prescribing rates elevate the risk of harm. Māori and Pasifika patients are at greater risk of healthcare harm. The extent of medication- related harm, and harm by ethnicity, is unknown in New Zealand general practice.

Determining the nature and extent of these harms is a first step to addressing these problems. Strategies to reduce harm increasingly involve patients. Providing risk information at an appropriate health literacy level can improve patient engagement.

Aims

1) To identify problems associated with medication use in New Zealand general practice

    a) To evaluate the extent of medication-related harm arising from prescribing in NZ general practice

    b) To evaluate an automated clinician alert system to see whether there were any inequities in clinician action taken based on patient ethnicity or other demographic factors

2) To explore strategies to improve medication safety in New Zealand general practice

    a) To explore what patients and prescribers would like in a decision support and communication tool

    b) To explore whether a tailored information package for patients can improve

knowledge of NSAIDs and reduce self-reported use of NSAIDs

Methods

This thesis used a pragmatic mixed-methods approach in four linked studies. The first two studies are analyses of general practice record review data. They outlined problems associated with medication use, by estimating the amount of medication-related harm, and by determining whether clinician action varies by patient ethnicity when notified of the harm. Studies three and four explored strategies to improve medication safety.

Patients and prescribers were interviewed in the third study to understand what they would like from a medication decision support and communication tool. The fourth study considered the feasibility of conducting a randomised controlled trial to test whether a tailored information package is acceptable and effective in improving knowledge of non-steroidal anti-inflammatory drugs (NSAIDs) and reducing self-reported NSAID use in patients at risk of renal damage.

Results

1. The estimated incidence rate of all medication-related harms in New Zealand general practice was 73.9 harms per 1000 patient-years, the estimated incidence of preventable or potentially preventable medication-related harms was 15.6 per 1000 patient-years, and the estimated hospitalisation rate was 1.1 per 1000 patient-years. Most harms were minor (1390/1762, 78.9%), but one in five harms were moderate or severe (373/1762, 21.1%); three patients died (3/9076, 0.03%). Most medication-related harms were not preventable (*n*=1432, 81.3%); the remainder were considered preventable or potentially preventable (*n*=330, 18.7%).

2. Analysis of whether clinicians took action following a risk alert found no evidence of a difference in the odds of having action taken by patient ethnicity, however the estimated odds for Māori and Pasifika patients were lower compared with Europeans (Māori OR 0.88, 95 %CI 0.63–1.22; Pasifika OR 0.88, 95 %CI 0.52–1.49). Females had significantly lower odds of having action taken compared with males (OR 0.76, 95 %CI 0.59–0.96).

3. Patients want as much information as possible about their medications and risk, but doctors find it difficult to communicate that information. Participants were cautiously optimistic about a prescribing risk assessment and communication tool, but worried about potential harm arising from its use. They also identified requirements for the tool and features to avoid. Culturally safe and trustworthy doctor-patient relationships are required before successful implementation of any tool.

4. Patients at risk of renal damage are willing to participate in a study via email recruitment, and engage with an interactive learning activity about non-steroidal anti-inflammatory drugs online. This randomized feasibility trial demonstrated that this research method is feasible for the purposes of recruiting patients and testing the effects of providing this targeted information package.

Conclusion

Medication-related harm in general practice is common. Patient and prescriber perspectives are needed to inform harm-reduction strategies. Use of a targeted alert system has potential to mitigate risk from medication-related harm. Clinicians typically take action on alerts arising from a general practice electronic alert system, but our study suggested that they

appear to take less action for women and Māori and Pasifika patients. Recognising clinician biases may improve the equitability of health care provision; respectful, culturally safe doctor-patient relationships are critical to the successful implementation of any risk-mitigation tool. Delivering medication-risk information to targeted patients online is feasible, and further studies are required to determine determine whether that improves knowledge or changes behaviour.

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Pandora

I was given a jar of pills
Containing ills of every description
A prescription I couldn't stomach
All that's left is Hope inside it

Hope - or deceptive expectation
Indisposed, with hope deferred
Referred now to another physician
Who just writes out another prescription.

(Doctors with egos of minor deities
contribute to the harms of polypharmacy).

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Glossary

Abbreviation	Explanation
ACC	Accident Compensation Corporation
ACE-i	Angiotensin-Converting Enzyme Inhibitors
AHRQ	Agency for Healthcare Research and Quality (US)
ARB	Angiotensin II Receptor Blockers
ATC	Anatomical Therapeutic Chemical classification system
bpac^{nz}	Best Practice Advisory Centre, New Zealand
CDSS	Computerised Decision Support Systems
CRTF	Clinical Research Training Fellowship
CTCAE	Common Terminology Criteria for Adverse Events
DHB	District Health Board
eGFR	Estimated Glomerular Filtration Rate, used to assess renal function
EHR	Electronic Health Record (see PMS)
GP	General Practitioner
GTT	Global Trigger Tool
HFE	Human Factors/Ergonomics
HQSC	Health Quality and Safety Commission New Zealand
HRC	Health Research Council of New Zealand
ICH	The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IHI	American Institute for Healthcare Improvement (US)

I-MeDeSA	Instrument for Evaluating Human Factors Principles in Medication Related Decision Support Alerts
INR	International Normalized Ratio, a standardised measure of how long it takes blood to clot used to measure the effect of anticoagulants
IoM	Institute of Medicine
LINNAEUS EURO-PC	Learning from International Networks about Errors and Understanding Safety in Primary Care
MedDRA	Medical Dictionary of Regularly Activities
MELAA	Middle Eastern, Latin American, or African ethnicities
MVSH	Multi-axial harms coding system: Mode (how did the harm occur), Variable (why did the harm occur), System (bodily or other system affected), and Harm (specific details of the harm).
NHS	National Health Service (UK)
NICE	The National Institute for Health and Care Excellence (UK)
NPSA	National Patient Safety Agency (UK)
NPT	Normalisation Process Theory
NSAIDs	Non-Steroidal Anti-Inflammatory Drugs
NZ	Aotearoa, New Zealand
OTC	Over The Counter - medication which can be purchased without a prescription
PCA	Patient Controlled Analgesia
PMS	Patient Management System (see EHR)

RCT	Randomized Controlled Trial
REDCap	Research Electronic Data Capture
RNZCGP	Royal New Zealand College of General Practitioners
SEIPS	Systems Engineering Initiative for Patient Safety
SHARP	The Safety, Harms, And Risk Reduction Project. Working title for *Patient Harms in New Zealand general practices: Records Review Study*
UK	United Kingdom
US	United States of America
WHO	World Health Organization

Te Reo Māori	**English Translation**
Aotearoa	New Zealand
Kia ora!	Hello! Cheers! (lit. translation: have life/health)
Mana	Authority, power
Te Tiriti o Waitangi	The Treaty of Waitangi
Whakamā	Shy, embarrassed
Whānau	Family

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Chapter 1 Introduction

1.1. Preface

This thesis aims to identify problems associated with medication use and to explore strategies to improve medication safety in Aotearoa New Zealand (NZ) general practice. This chapter introduces the context of medication safety in NZ general practice. The origins of the patient safety movement are described and patient safety terminology is defined for subsequent use in this thesis. Methods to measure patient safety are discussed, together with their limitations. The context of NZ general practice is outlined together with a brief history of ethnicity and health equity in NZ. The rationale for concentrating on medication safety in general practice is explained. The development and use of current patient safety strategies are described, including systems theory, patient safety tools and technologies and informed consent and health literacy. The final section describes the development of this thesis and presents its aims and methods.

1.2. The patient safety movement

The recognition that patients may be harmed by medical care is not new. In the early 1800s, Drs Oliver Wendell Holmes and Ignaz Semmelweis independently recognised poor hand hygiene was responsible for puerperal fever, although their findings were misunderstood or rejected by most of their medical colleagues.[1] Frequently misattributed to Hippocrates or Galen, it was around this time the phrase "*primum non nocere*" (Latin: first, do no harm) was coined by the French physician Chomel.[2]

In the second half of the twentieth century, the rapidly expanding arsenal of largely untested diagnostic procedures and medical treatments were recognised to be causing patient harm.[3-7] It was not until the 1990s that patient safety was considered an important facet of healthcare systems, following the publication of the Harvard Medical Practice Study,[8,9] and the subsequent highly influential report from the United States Institute of Medicine: To Err is Human.[10,11] The main recommendations arising from that report established a model for patient safety across the US health system, from government, to individual healthcare organisations, to individual patient encounters (Box 1-1).

Box 1-1 Key recommendations from To Err is Human[10]

- Establish a national group to enhance safety by developing leadership, research, tools and protocols
- Develop mandatory and voluntary reporting systems to identify and learn from errors,to continuously improve patient safety
- Raise safety standards and expectations for safety improvement through organisations providing oversight (e.g., funders and professional groups)
- Implement safe healthcare delivery practices and safety systems in healthcare organisations

Following the publication of that report, research and advisory groups dedicated to patient safety were established around the globe. At least partially in response to this, in 2001 the Agency for Healthcare Research and Quality (AHRQ) was founded in the US,[12] and the National Patient Safety Agency (NPSA) in the UK.[13] The World Alliance for Patient Safety was founded in 2002 by the World Health Organization (WHO).[14] These groups raise the awareness and support quality and safety improvements in smaller healthcare

organisations, including guideline development agencies, therapeutic regulatory agencies, and professional clinical bodies.

Healthcare quality and safety is now placed at the forefront of the health systems of all developed countries, probably due to the recognition of the cost of patient harm. Fatalities and serious harms cause the greatest social and economic burden; serious adverse events arising from primary and secondary care have been estimated to account for 3.2% of total health loss from all causes in NZ.[15] While it is difficult to calculate the exact burden of patient harm due to additional health and social costs arising from impaired function and life lost, averting even a few preventable fatalities or serious harms is likely to yield significant savings, besides any moral imperative for attempting to do so.[16]

1.2.1. The patient safety movement in New Zealand

The NZ government established the Health Quality and Safety Commission (HQSC) in 2010, after noting NZ had made only "modest improvements in health quality and safety" compared with other similar countries.[17] The purpose of the HQSC is to provide a coordinated effort on quality related activities. It works with clinicians, providers and consumers to improve health and disability support services, aiming to reduce patient harm from healthcare associated infections, surgery, medication, and falls.[18]

Another strong driver for patient safety in NZ is the Accident Compensation Corporation (ACC), which provides NZ's unique universal no-fault insurance cover for injury. ACC was established in 1972 to cover all injuries to employees and motor vehicle injuries.[19] ACC cover has expanded over time, and since 2005 all treatment injuries have been covered. Treatment injury is defined as a personal injury sustained while being treated by a registered

health professional.[20] ACC spent around $480 million NZD on treatment injury claims in the 2018/19 financial year and is strongly motivated to reduce its liability in this area.[20] ACC therefore provides substantial funding for treatment safety programmes, investing $45 million between 2017 and 2022 to prevent treatment injury, such as its education programme for prescribers and patients aiming to prevent Foetal Anticonvulsant Syndrome (FACS).[20]

1.2.2. Defining patient safety

Patient safety terminology is confusing. Harm may be described as a patient safety incident, or an adverse, serious, or sentinel event. At other times harm is used synonymously with error. Patient safety incidents, such as delivering the wrong dose of medicine to a patient, do not necessarily result in harm, but are comparatively easy to measure in the context of electronic prescribing and dispensing. The lack of shared definitions causes challenges in reading and interpreting patient safety literature.[21] A multidisciplinary approach to developing a shared definition is consistent with current recommendations by WHO, and others.[22-25]

The World Health Organization has organised patient safety language in the *Conceptual Framework for the International Classification for Patient Safety*.[22] This framework was primarily derived from hospital-based research. It has been criticised for lack of sensitivity for application in general practice settings, particularly in the classification of harm severity.[26] WHO defines harm as "impairment of structure or function of the body and/or any deleterious effect arising there from. Harm includes disease, injury, suffering, disability and death."[22]

Box 1-2 The importance of shared patient safety definitions.

> *"The importance of being able to classify more consistently the major concepts associated with patient safety cannot be underestimated… The consistent use of keypatient safety concepts with agreed definitions and preferred terms, in conjunction with a comprehensive but adaptable classification, paves the way for the systematiccollection, aggregation and analysis of relevant information. In short, classification must be deeply integrated in all work on patient safety around the world"*
>
> Sir Liam Donaldson[23]

Patients typically define harm more broadly than clinicians.[27] A comprehensive understanding of harm should include both physical and emotional harms, delays in treatment associated with extension or worsening of poor health, inconvenience, and additional financial costs to patients.[28] The WHO definition can be expanded to include those features (Box 1-3). This broad definition of harm will be used throughout this thesis.

Box 1-3 Harm defined[28]

> "*Patient harm is physical or emotional negative consequences to patients directly arising from health care, beyond the usual consequences of care and not attributable to the patient's health condition*."

Patients and their families are the primary victims of healthcare-related harm. The term "second victim" has been used to describe healthcare workers, rightly recognising the

emotional impact of patient harm on clinicians.[29] Despite widespread understanding and use of "second victim," this term has been criticised as it distracts attention from the primary victims, may reduce the impetus for patient safety research, and may subtly help clinicians and organisations avoid responsibility.[30,31] However, a truly holistic definition of healthcare-related harm would include primary and secondary victims, as well as factors such as environmental contamination from chemical leakage and the ethical dilemmas associated with pharmaceutical funding decisions. An holistic approach is congruent with a Māori worldview and perspective of health, which acknowledges a far greater degree of interrelatedness between all things than non-Māori perspectives.[32] For example, Western thinking values health mainly in terms of personal wellbeing and socio-economic output, while Māori concepts of health include physical, mental and spiritual dimensions as well as whānau (family) and community wellbeing.[32] Such a definition of health-care related harm is beyond the scope of the thesis, but should be held in mind when considering healthcare harms in NZ.

1.2.3. Measuring patient safety

In addition to difficulties associated with a paucity of defined patient safety terms, measuring patient safety is challenging. Adverse events are seldom directly observed in general practice settings, because patient contact in general practice is brief and medication is typically administered off-site. Harm in general practice settings is typically recorded if a patient complains to a clinician about it, and if that clinician considers it worthy of documentation.[33] Additionally, patients face barriers to accessing healthcare and to reporting harm.[34-36] Despite these limitations, attempting to measure patient safety in some form is a laudable aim. Traditional methods of measuring patient safety include incident

reporting, use of trigger tools, and use of routinely collected data.[21,37,38]

Incident reporting relies on clinicians recording events in some type of organisational database for review and evaluation. Use of incident reporting systems depends on multiple factors, including ease of use of the reporting system (including accessible technology), clinician time and motivation. The patient safety culture of the organisation, namely, the shared values, staff attitudes and behaviour play an important role in incident reporting.[39,40] Incident reporting systems vary greatly depending on healthcare setting; they are typically underdeveloped in general practice settings where use depends on practice safety culture.[41] They are prone to underreporting, and report analysis and subsequent learning is hindered.[33,42]

Medical record audits aim to detect patient harm in a systematic way. The Global Trigger Tool was developed by expert consensus in 2003 by the American Institute for Healthcare Improvement (IHI), for hospital use as a rapid retrospective record audit tool.[38] Medical records are checked by trained reviewers for "triggers": factors that increase the likelihood of harm being present. Examples of triggers include INR>6.0,[a] glucose <3.5mmol/L,[b] and falls.[38] Charts with triggers are systematically reviewed for patient harms.[38] Trigger tools help both detect and monitor patient harm rates throughout the health system. They may be used to compare harm rates over time and between organisations, and can help prioritise safety improvement measures and resource allocation.[38] Trigger tools have now been

[a] INR = International Normalised Ratio, a standardised measure of how long it takes blood to clot. It is usedto measure the effect of anticoagulants (particularly warfarin). The therapeutic range is usually around 2.0-3.5, depending on the condition. An INR of 6.0 or more indicates a higher risk of bleeding.

[b] Blood glucose levels should be above 4.0mmol/L. Low blood glucose levels (hypoglycaemia) may cause confusion, coma and death. Hypoglycaemia is usually caused by medication, especially insulin.

adapted for use in other countries and healthcare settings, including NZ general practice.[18,43-45] Trigger tools are becoming increasingly sophisticated as they incorporate technological advances, such as improving automating and electronic record scanning using natural language processing.[46,47] The trigger tool is an important first step in developing a tool to measure patient safety in general practice, although this method is incapable of measuring harms which are not "flagged" by the trigger review method. Trigger tools monitor harm rates and may enhance patient safety culture, but unless used prospectively, they are unable to prevent harms from occurring.

Data collected for other purposes also provide insight into adverse events.[37] Record review studies involve in-depth examination of clinical records, scouring these for evidence of patient harm, or other patient safety issues (e.g., inappropriate prescribing). Record review studies are time and personnel intensive.[48] They can provide unique insight into a patient's journey of care and in-depth analysis of causal factors,[49] but the quality of the review depends on the quality of the records.[33] Evaluation of this method has found it typically lacks rigor and reproducibility,[50,51] and yet it remains the main way of assessing national adverse event rates.[52] Evaluation of third party data, such as insurance claims, is another method of evaluating patient safety.[53,54] This method provides some information, but is further removed from the source data, is skewed towards more severe patient harms, and all the limitations of the above methods are compounded.[54,55]

Composite measures of the above methods, as well as using automated evaluation methods proposed by technological advances are likely to provide a more comprehensive evaluation of patient safety over time.[52,56] Until there is wider acceptance of shared definitions and validated methodologies, the ability to measure and compare patient safety parameters

remains severely limited. In the meantime, researchers must acknowledge the limitations of their chosen methodology to assess patient harm across the health system.

1.2.4. New Zealand general practice - worthy of patient safety attention

General practice is the usual first point of contact for patients seeking healthcare and provides a gateway to accessing the rest of the NZ health system.[57] Care is delivered predominantly in community general practice clinics by health professionals including general practitioners (GPs), practice nurses, nurse practitioners, pharmacists and other health professionals. General practice provides diagnostic and treatment services, health education, disease prevention and screening. Clinicians routinely use electronic health records to facilitate patient care. Patients increasingly can access at least some of their records and interact with their clinicians online via secure patient portals (e.g., view test results, book appointments and request repeat prescriptions). There are some linkages between primary and secondary care IT services; it is anticipated these will improve over time as the government has committed over $515 million in the 2021 budget to develop effective health infrastructure, including a national health information platform.[58,59] NZ general practice faces similar issues to other developed nations – increasing longevity is increasing the complexity of our patients, who have increasing multimorbidity and polypharmacy.[60-63]

NZ has a dual public-private health system. NZ general practices are typically run as small businesses, usually owned and operated by general practitioners.[64] Most general practice healthcare is partly subsidised by the government on a capitation basis (i.e., practices receive annual funding per enrolled patient, calculated quarterly). Accident care is partly

funded by the national ACC scheme. A patchwork of targeted funds is administered regionally at present and is applied to some patients and conditions on a variable basis (e.g., extra funding for high-needs patients, free cervical smears for Māori and Pasifika women, free maternity care for women in the first trimester, removal of some complex skin lesions, etc.). Around 33% of New Zealanders have private health insurance.[65] Those who do usually only have cover for hospital care for elective surgery (e.g., cataracts, joint replacements etc.), which paradoxically places additional strain on the public health care system.[66] Patients 14 years and older have to pay an out-of-pocket co-payment to receive general practice care and medication. These co-payments limit access to care, and exacerbate inequity.[64,67] Patients can apply for a Community Services Card from the government, which reduces medical and prescription fees.

Most patient safety efforts concentrate on hospital care, rightly recognising that hospitals are places where patients are typically sicker, where more invasive investigations occur and more risky treatments are administered. However, more healthcare in NZ is delivered in general practice than any other healthcare setting. Each year, nearly 80% of New Zealanders visit their GP at least once; the population average is 2.9 visits per year.[68] In comparison, only around 24% of the population are hospitalised per year (latest figures are available only for the 2017-18 year: age-standardised publicly-funded hospitalisation rate of 224 discharges per 1000 patients, privately-funded hospitalisation rate is 17 per 1000).[69,70]

General practice has traditionally been regarded as a low-risk environment for patient harm,[71] although the patient safety data available to date indicate that harm arising from general practice has probably been underestimated.[72] While few dangerous investigations or

treatments are administered in general practice, prescribing rates are high. During the 2015-16 year, nearly 80% of enrolled general practice patients received at least one prescription item, and NZ GPs prescribed more than 42.4 million prescription items, or 9,715 items per 1000 patients.[73] High patient volumes and high prescribing rates in general practice consequently represent a high risk of causing harm, although the risk of harm per individual patient is likely to be low.[72]

Improving patient safety in general practice is a priority for international and local health systems. Patient safety in general practice is increasingly important as more healthcare services are transferred from secondary to primary healthcare settings.[74] The most common services transferred to primary healthcare to date include lower risk activities such as minor surgery, intra-uterine device insertion, diabetes care, and sleep apnoea care.[75] This transfer of services to primary care presents both new clinical risks and also organizational safety risks, such as increased workload and administration-related safety issues. Should this trend continue, patient safety in general practice will require increased attention.

Without a clinical perspective, it is probably hard to understand why addressing patient safety in general practice is so difficult. Box 1-4 aims to provide some insight into the work of a general practitioner, inspired by Aneez Esmail.[76]

Box 1-4 Grassroots general practice in New Zealand

> I work in a small suburban clinic, in a poor part of town. Many of my patients can't afford to see me, even though it's only $19.50 NZD with a Community Services Card (or $25-$43 without one). They can't afford the $5 per item prescription charge per item either. We're all grateful for the new mega-chemists that somehow operate without

charging a prescription fee, but they are in town, and it's a $5 return trip on the bus. Naturally my patients save up their problems before they come and see me, so each 15 minute appointment is bursting with problems. Sometimes their presentation is so delayed that they are extremely unwell and require urgent secondary care, or they are just a lot sicker than they need to be. Some people I've referred months ago but they are getting worse waiting for their hospital appointment. My day is frequently interrupted with phone calls and stymied by technological issues limiting my ability to access critical patient information or complete paperwork. Around 10% of my patients don't speak much English, but instead rely on interpreters or family to communicate. My patients are usually kind, respectful, and in good humour. Other patients are hostile and aggressive, demanding tests I can't order, and medication they don't need. In this time-pressured and resource-limited setting I need to carefully listen, examine, test, refer, diagnose, and treat my patients with care and compassion.

I also advise people about what they have read on the internet, encourage the reluctant to have invasive screening tests or vaccinations, navigate the tensions between estranged parents bringing their shared-care child for review, respond to criticisms about my colleagues, tell people they are unfit to drive, write insurance reports, keep abreast of medical developments, never miss anything, and never make a mistake. My prescribing is entirely "evidence based" from current clinical guidelines. I calculate the risks and benefits of each medication for each patient. My patients are fully informed about their medications, and have the capacity to actively participate in shared decision-making discussions about their treatment...

Of course, most of the time my GP colleagues and I just do the best we can. The

concept of "satisficing" – "*settling for… management that that is satisfactory and sufficient*" while relying on relational continuity to address long-term problems over time, seems apt.[60] In short, life at the grassroots is muddy. I keep my boots on.

The complexity of prescribing in the real world is highlighted in the following vignettes by NZ GPs.

"*On Sunday I get a call from an elderly patient. Her husband is dying of bowel cancer. He cannot sleep. I started him on a sleeping pill to help a month ago. Recently she has seen a programme on television about how people who take sleeping pills die earlier than those that don't and so she has stopped it and her husband is up half the night again which means she is as well. I promise to visit but I wonder why I am, 'Heck, he's dying. Why not sleep well?' When I get to the door I knock three times but no one hears me. I go back to the car and call my patient to say I am there. She lets me in and we talk for a long time about randomised controlled trials and what can be inferred and the inevitability of her husband's illness. She encourages and nods and nods and encourages until I remember she is deaf on the side I am talking to. She is not sure what I am saying but she thinks it is her husband's own fault he doesn't sleep because he stays up to watch rugby and she says to lie down and close his eyes and think of God and what do I think? I smile and say it is ok to take the pill. She says that's good then.*"
Dr Glenn Colquhoun[77]

"*Beside his bed there is a small china egg cup containing two pills and two capsules. 'They are my wake-up ones, before breakfast,' he informs me. 'And where are your night ones?' I ask. I am relieved to see a plastic pack with a compartment for each day*

of the week. But when I open it, Monday has Thyroxine, Tuesday Omeprazole, Wednesday Zopiclone, Thursday and Friday Laxsol, but Saturday and Sunday are unidentified. 'What are these ones?" I ask. He replied: 'I think they are spares. I like a few spares… I've got my own system and it works.'" Dr Lucy O'Hagan[78]

1.3. A brief history of ethnicity and health equity in New Zealand

NZ's history and colonial legacy has a huge impact on the health of New Zealanders. The following synopsis explains why evaluating equity by ethnicity is a vital component of health research in this country.

Aotearoa NZ, home to the indigenous population of Māori, was colonised by Britain from the mid-19th century. The founding constitutional document, Te Tiriti O Waitangi (The Treaty of Waitangi), was signed in 1840 by representatives of the British Crown and Māori leaders. It enshrines the ideals of equity and protection of Māori.[79] Te Tiriti O Waitangi was not honoured by the early British colonists. Similar to other indigenous peoples, Māori land was confiscated, Māori children were taken from their families, and Māori culture and language were suppressed. The Māori population was further decimated through warfare, disease, urban drift and cultural disassociation.[80]

Early settlers envisaged NZ as a "better Britain" where an egalitarian society could flourish (unless you were Māori or a woman).[81,82] British and Irish people could freely immigrate to NZ until the 1960s. Traditional social and economic ties with Britain were greatly weakened when Britain joined the European Economic Community in 1973. This generated interest in

establishing a NZ national identity and a renewed commitment to the Principles of the Treaty, still articulated by most public institutions today.[80] NZ has a legislative commitment to biculturalism, but in reality it is a multi-ethnic country, which practices "de facto multiculturalism."[80,83] The main ethnic groupings used in NZ health research are European, Māori, Pasifika (Pacific peoples), Asian, MELAA (Middle Eastern / Latin American / African) and "Other ethnicity" (all other ethnicities not previously specified).

NZ in 2021 has a population of 4.9 million people. The majority are descendants of those original British and Irish settlers, with 70.2% of the population identifying as European.[84] Europeans have better health and socioeconomic advantages than other ethnic groups. This is most starkly evident in life expectancy; Europeans live for approximately 7.5 years more than Māori and 5.5 years more than Pasifika.[85] In the 2018 Census 16.5% of the population identified as Māori.[86] Māori are over-represented in nearly every adverse statistic, experiencing worse health and more deprivation than other ethnic groups in NZ.[86,87]

Pasifika refers to people living in NZ who identify with the Pacific islands because of ancestry or cultural heritage; the term represents more than 40 different ethnic groups including Samoan, Tongan, Cook Islands Māori, Niuean, Fijian, Tokelauan and others. People from the Pacific Islands have been travelling to NZ for employment and education opportunities for the past 150 years. In boom times, Pasifika were recruited to work in NZ, but in economic downturns they have been harshly and unfairly treated.[88] In 2018 Pasifika made up 8.1% of the population.[89] Like Māori, Pasifika are also over-represented in adverse health and socioeconomic statistics.[90]

The first Asian immigrants to NZ were Chinese gold-miners who arrived in the 1860s. Government legislation actively discriminated against Chinese immigrants from 1881- 1986;

Chinese were ineligible for naturalisation (citizenship) until 1951.[91] Since the 1990s NZ has had a policy of competitive migration and actively sought skilled Asian migrants.[83] On the other hand, waves of xenophobia and racism have disproportionately targeted people of Asian descent and influenced NZ policy.[83,92,93] In the 2018 Census 15.1% of the population identified as Asian.[84] People of Asian ethnicity generally experience good health and life expectancy, with new immigrants experiencing better health than those born in NZ.[94] A lack of attention to Asian health in the health sector is of concern as this population group grows; recognising the ethnic diversity within this group may clarify health issues for sub-groups.[94,95]

MELAA people make up only 1.5% of the population, and Other ethnicity 1.2%.[84] People from the Middle East are the largest subgroup, with nearly 28,000 people as at the 2018 Census.[84] Many recent immigrants in this group are refugees, who have a unique set of complex health needs.[96] The terrorist attack on March 15 2019 brought decades of anti-Muslim and anti-Arab prejudice to light.[97] People of MELAA and Other ethnic groups are largely ignored in the health literature due to their statistically marginal contribution to the data.

Equal opportunity for all New Zealanders is enshrined in NZ law and health policy.[98] Addressing the nefarious legacy of colonisation, assimilation, and pervasive structural racism in health is beyond the scope of this thesis. NZ researchers have an obligation to evaluate healthcare interventions in terms of ethnicity, in order to ensure they do not exacerbate health inequity.[99,100] New Zealanders can identify with multiple ethnicities, but prioritised ethnicity is used in the health sector and in this thesis.[101]

Box 1-6 Equity defined

> *"In Aotearoa New Zealand, people have difference in health that are not only avoidable but unfair and unjust. Equity recognises different people with different levels of advantage require different approaches and resources to get equitable health outcomes."* Ministry of Health[98]

1.4. Medication safety in general practice

The rationale for considering patient safety in general practice was addressed above. Prescribed medications comprises the bulk of treatment administered in general practice, so medication safety should be a priority for patient safety efforts in this area. High prescribing rates in general practice increase the risk of patient harm from medication. One way to measure the extent of serious medication harm in general practice is by examining hospital admissions. Up to half of all hospital admissions in one international meta-analysis were attributed to adverse medication events; higher rates were observed in studies focusing on older people.[102,103] A European review of publications from 2000-2014 found 3.5% of all admissions on average were caused by an adverse drug reaction.[104] A review of Australian literature from 2008-13 found 2-3% of all hospitalisations were medication- related.[105] In NZ, a 2014 study found nearly a third of acute medical hospital admissions were related to adverse medication events.[106]

Hospital admissions reflect only the most serious medication-related harms. Measuring the true extent of medication-related harm in general practice is difficult. Firstly, the harm will be recorded in the patient records only if the patient complains to their healthcare provider

about a problem, and if the provider then considers the patient complaint sufficiently serious to do something about it. Secondly, the provider may record a medication harm in several ways; for example, nausea with antibiotics may be considered a minor side-effect and hence may not be recorded, more serious adverse reactions may be recorded in the general notes or as “medication warnings”, and unusual reactions or those involving new medications may be reported to Centre for Adverse Reactions Monitoring (CARM). Thirdly, non-physical medication harms are unlikely to be recorded at all; for example, the hassle, expense and time wasted in obtaining a correct prescription in the case of a prescribing or dispensing error is all borne by the patient, yet is seldom acknowledged.

Estimating medication-related harm in general practice is therefore fraught with difficulty; comparisons between studies are hampered by methodological variability and paucity of shared definitions. A comprehensive meta-analysis of published and unpublished international studies from 1980-2014 found up to 24 safety incidents per 100 consultations (the median incident rate for each study was 2-3 per 100 consultations); diagnostic and medication-related incidents were most likely to be associated with patient harm, with 8-11% of medication-related incidents resulting in patient harm.[107] A systematic review of published international literature estimated the incidence of preventable adverse drug events as 15/1000 person-years.[108]

Similarly, comparisons of country-specific data are difficult due to the broad range of outcome measures. For example, a survey of Australian general practice patients over 45 years old found 11.6% patients reported an adverse drug event in the preceding six months.[109] The incidence of avoidable significant harm in general practice in England is 35.6 (95% CI 23.3 to 48.0) per 100 000 patient- years; medication-related problems accounted for

a quarter of these harms.[110] In a cross-sectional mixed methods analysis of patient safety incidents in England and Wales, medication-related incidents accounted for the greatest proportion of incidents (31%, and 15% of serious harms).[111] In a retrospective general practice record review study in the Netherlands 5.8% of patients experienced harm; 14.7% of adverse events detected related to medication.[71] And a Swedish study examining both primary and secondary care records found a prevalence of adverse drug events of 12% (95%CI 11.1-12.9%).[112]

1.4.1. Epidemiology of harm in New Zealand general practice

To improve knowledge of patient harm arising from general practice in NZ a general practice record review study was undertaken (Patient harms in NZ general practices: Records Review Study). The general practice records of 9076 randomly selected general practice patients from 2011 to 2013 inclusive were examined.[28,113] These records provide a window on the whole health system; as well as detailed accounts of general practice care, they provide information about patients' key hospital experiences.

Using the definition of harm outlined above, it was found that 1505 patients (16.6%) experienced at least one harm in the three year study period; when study results were weighted to the NZ population this is equivalent to 18.0% of all NZ general practice patients experiencing harm.[113] The estimated incidence of harm was 123 per 1000 patient-years. Some patients experienced multiple harms during the study period. While most harms were minor, one in four harms were considered moderate or severe. Harms included medication reactions, wound infections, falls, hospitalisation, intracerebral bleeding and death. Harm from medication prescribed in general practice accounted for most of the harm (1762/2972, 59.2% of all harms). I used the data from that study to

independently conduct a detailed analysis of the medication-related harms identified. Results are presented in Chapter 2.

1.5. Strategies to improve medication safety

Since 2004, WHO has initiated three Global Patient Safety Challenges. Recognising the harm arising from medication, the Third Global Patient Safety Challenge was launched in 2017 - Medication Without Harm.[114,115] The overall goal of this Challenge is "improving medication safety by strengthening the systems for reducing medication errors and avoidable medication-related harm."[115] WHO aims to reduce the amount of severe, avoidable medication-related harm across the world by 50% over 5 years.[115] So far WHO has identified priority areas for improving medication safety, and has developed medication safety resources for patients and clinicians.

WHO has laid out a five-point strategic framework for addressing the Global Patient Safety Challenge on Medication Safety at international, national, and local levels. Of particular relevance to this thesis is their final strategic objective, which is to "empower patients, families and their carers to become actively involved and engaged in treatment or care decisions, ask questions, spot errors and effectively manage their medications."[115] They aim to do this by putting "mechanisms in place, including the use of tools and technologies, to enhance patient awareness and knowledge about medicines and medication use process, and patients' role in managing their own medications safely."[115]

1.5.1. Systems theory

Other industries have successfully improved safety by taking a systems perspective. As early as 1960 the psychologist Alphonse Chapanis, famous for redesigning cockpit controls and

improving aviation safety, concentrated on medication-related errors in hospital care.[116] Chapanis identified four areas which required attention, namely communication, medication procedures, the working environment, and training and education.[116] Much of the learnings from his research remain relevant today, yet many of the issues that were identified sixty years ago remain unaddressed, and patient harm from medication still occurs worldwide.[114]

The systems theory of healthcare safety acknowledges "most healthcare problems and solutions belong to the system."[117] The health system is complex, interrelated, and context-specific.[118,119] Complex systems consist of multiple interactive relationships between people, work, technology, organizational structures, and internal and external environmental factors.[120] Healthcare provision is susceptible to both variability in demand and resource constraints, which increases the complexity of creating and maintaining safe systems. This variability also exacerbates the intrinsic goal conflict associated with healthcare provision.[120] Goal conflict refers to the idea that being efficient (tasks should be completed using the minimum of resources required) and being thorough (tasks should only be attempted if sufficient resources are available to complete them safely) are irreconcilable goals.[121] Goal conflicts in a variable complex system inevitably result in adaptation of work processes, leading to a difference between "work-as-imagined" (what is in the procedure manual) and "work-as-done" (what we actually do around here to get the job done, which may include procedural violation).[120,122] If "work-as-done" is normalised without adequate safety considerations, then over time an organization will migrate towards an accident-prone system.[122] In short, understanding safety requires examination of not just the system components and outcomes (both good and bad), but also interactions within the system and the adaptations required to undertake everyday work.[120]

Resilience Engineering for safer systems requires the tensions between efficiency and thoroughness be balanced in order to both anticipate and respond to patient safety threats.[121] Resilience Engineering defines success as the capacity to anticipate and plan for changing risk parameters before harm occurs.[122] A systems approach to healthcare safety incorporates the following five principles: first, multiple perspectives are required to understand the system; second, working conditions (i.e., requirements, demands, supply, constraints) are acknowledged; third, interactions and workflow are analysed; fourth, professional decisions are reviewed to understand why they made sense within the context of the system; fifth, successful system change is analysed to recognise what was actually required to achieve success.[117]

The Systems Engineering Initiative for Patient Safety (SEIPS) model is a human factors/ergonomics (HFE) framework for studying and improving health and healthcare, underpinned by three principles: systems orientation, person centeredness, and design-driven improvements.[123] Traditional patient safety efforts rely heavily on education and subsequent behaviour change, probably overestimating the capacity of individuals to change, while underestimating organisational factors. HFE addresses problems by redesigning the system so it is resilient to unanticipated events, so the most intuitive and logical decision is the correct action to take for end-users. HFE strategies attend to factors ranging from the individual to the organisational level.[124] Figure 1-1 provides a model of a SEIPS approach to describing the pathway of an elderly patient obtaining a repeat prescription by phone for antihypertensive medication during a Covid lockdown.[125] (As it happens, this hypothetical patient was overdue a blood-pressure assessment and had not been taking her medication for a few months due to cost, and because her pills make her

feel dizzy. Her daughter found out and was concerned; she encouraged her mother to ring up for a repeat prescription. This patient was advised to come in for a blood-pressure check, but declined as she was afraid of catching Covid in the practice). Consideration of all these factors helps explain why the suboptimal prescribing occurred, resulting in patient harm. Figure 1-1 depicts multiple components and multiple points of interaction. Any one component or action in that model could be examined and potentially improved to attempt to reduce the medication-related harm.

Systems theory research involves building and using explicit models to explain cause-and-effect.[122] These models can be tested and calibrated with data and repeated by others.[126] System-level decisions also affect whether new innovations are adopted, spread, or are implemented.[127] Examples of systems factor thinking relating to medication include developing and testing computerised prescribing systems, patient controlled analgesia (PCA) pump review, and emergency medication draw redesign.[128,129]

Implementation science is related to systems theory research. Implementation science aims to improve healthcare quality by examining the methods of promoting the uptake of evidence-based practices into routine use.[130] Implementation science is particularly useful when considering how to best embed use of a new tool into routine workflow by taking a systems approach to assess all aspects of the tool and workflow. One implementation science theory, Normalisation Process Theory, is further discussed in Study 3 (Chapter 4), in which general practitioners and patients were interviewed on their opinions about a patient safety tool.

1.5.2. Patient safety tools and technologies

Many methods of improving patient safety have been trialed, including audit, best practice guidelines, electronic alerts and reminders, clinician education, and addressing patient safety culture, but it is unclear which of these are the most effective.[131-133] Electronic prescribing is now well-recognised to improve the quality of prescribing and reduce prescribing errors.[134] Simple automated alert systems for electronic prescribing show warning messages of interactions between concurrently prescribed and long-term medications, as well as known drug allergies. Typically, potential interactions are over-reported, so some alerts are clinically meaningless and the frequency and volume of warning messages can be overwhelming - leading to "alert fatigue."[135-138] Prescribing software vendors limit alert modification because of concerns of potential liability should a medication harm subsequently occur.[139]

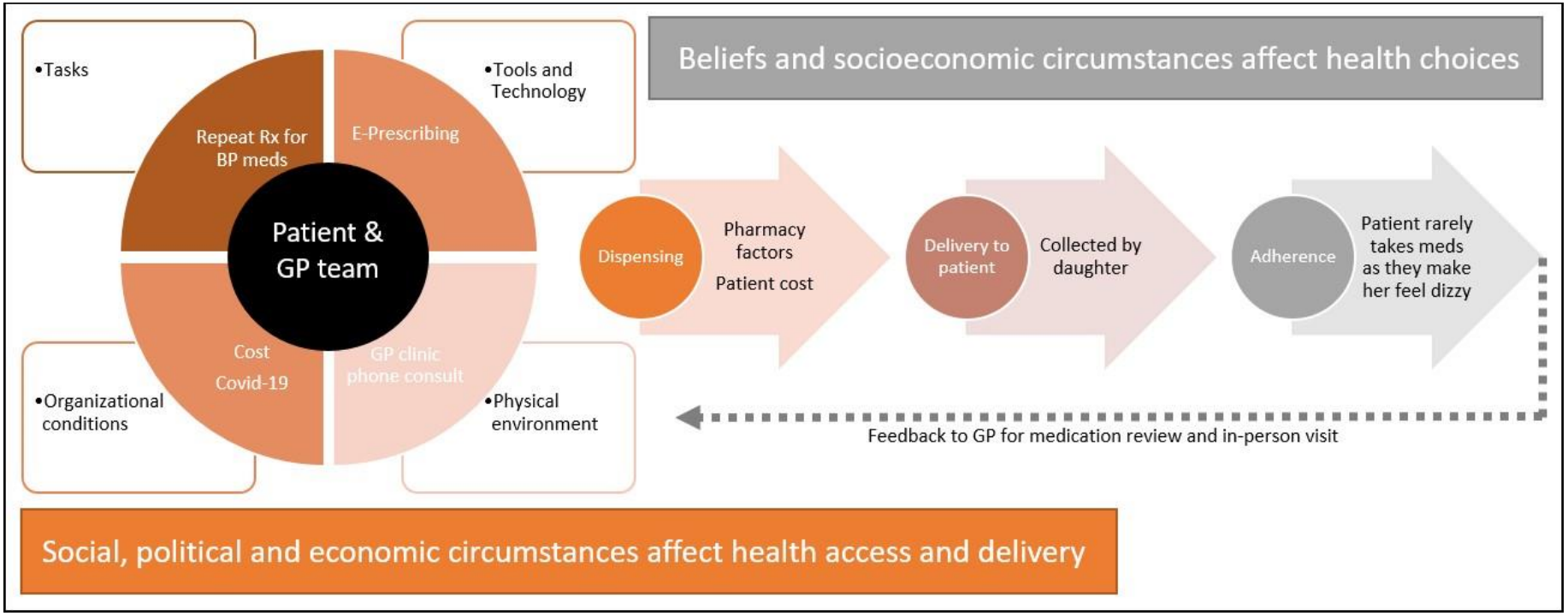

Figure 1-1 SEIPS model of a socio-technical systems approach for a patient obtaining a repeat prescription for anti-hypertensive medication during a Covid lockdown

There are a range of computerised decision support systems available to improve safe prescribing.[140] The most sophisticated systems are completely integrated with the electronic health record and automatically pre-populate with patient data. They are highly relevant to the task at hand (e.g., checking the renal function and INR of someone transitioning from warfarin to dabigatran). They automatically pop up at the time of prescribing, rather than relying on clinician motivation and time to use, and they may require manual input before the clinician can proceed and generate the prescription (e.g., check-box ticks required for the following statement: "I have checked the patient is using reliable contraception, and have counselled them about the risks of pregnancy while taking isotretinoin (a highly teratogenic medicine)"). A systematic meta-review of decision support software found only weak and inconsistent evidence of improvements in safer prescribing.[135] Evidence regarding patient outcomes is inconsistent, suggesting only modest benefits at best.[135,141,142] Decision support technology can be evaluated from a human factors perspective, such as by using the Instrument for Evaluating Human Factors Principles in Medication Related Decision Support Alerts (I-MeDeSA), which has some limitations in its design and scoring system.[143,144]

The most useful tools will become increasingly tailored to recognise individual patient risk (e.g., by including parameters such as renal function to estimate risk more accurately), or recognise the complexity of multimorbidity and polypharmacy, and provide meaningful feedback in terms of suggested medications for deprescribing trials. They will build on the evidence of successful clinical decision support tools.[145]

One such tailored alert system has been developed by the NZ health informatics company Conporto Health. The Conporto Event Detection and Mitigation alert system (Conporto EDM) is a warning system to alert clinicians when their patients are at higher risk of

experiencing harm from medication.[146] Their proof-of-concept trial demonstrated that clinicians do note these warnings and take remedial action, but there was concern that there was inequity in action taken when evaluated by patient ethnicity.[147] Detailed evaluation of the Conporto EDM proof-of-concept trial is reported in Study 2. Conporto Health also participated in the randomised feasibility trial discussed in Study 4.

1.5.3. Informed consent and health literacy

All prescribing is a tension between risks and benefits. Prescribers have a moral and legal obligation to ensure patients are fully informed about those risks and benefits (Box 1-7 contains selected points from the Medical Council of New Zealand's Statement on good prescribing).[148-150] Despite specific training, clinicians generally have poor understanding and low confidence in their ability to interpret statistics.[151,152]

While there is a good body of evidence outlining specific steps to improving shared decision making between clinicians and patients,[153-155] this process can still be challenging due to language and low health literacy. Health literacy is the ability to obtain, process and understand health information in order to make informed and appropriate health-related decisions.[156] Health literacy has been identified as a cause of health disparities,[157] and decision support tools can help address deficits in health literacy.[158]

Box 1-7 MCNZ Statement on good prescribing practice (selected points)[150]

"Ensure that the patient (or other lawful authority) is fully informed and consents to the proposed treatment and that he or she receives appropriate information, in a way they can understand, about the options available; including an assessment of the expected risks, adverse effects, benefits and costs of each option."

"Satisfy yourself that the patient understands how to take or use any medicine prescribed and is able to take it or use it."

"Periodically review the effect (benefits and harms) of the treatment and any new information about the patient's condition and health if the treatment is being prescribed for an extended period of time. Continuation or modification of treatment should depend on your evaluation of progress towards the objectives outlined in a treatment plan."

New Zealanders typically have low levels of health literacy – over half of adults surveyed had skills "insufficient to cope with the health literacy demands they typically face."[159] When these results were broken down by ethnicity, 75-80% of Māori and 90% of Pasifika had low health literacy levels.[159] Māori and people who are socioeconomically disadvantaged are disproportionately affected by adverse events and by harms arising from healthcare, including mortality, injury, and disability.[15,160-162] Māori and socially disadvantaged patients were found to be at higher risk of polypharmacy in a study of older New Zealanders.[62] To fully engage in patient-centred care, patients need to understand

their health information and risks. This will enable patients and their whānau to meaningfully participate in shared decision making.

1.6. Rationale for research

In order to address some of these issues, the following research question was proposed: How can medication safety in NZ general practice be improved? To answer that question, we need to understand how much medication-related harm is occurring, and whether any of that harm is preventable. Ethnicity is associated with inequitable health outcomes in general – but we do not know if this is true in general practice too. Once the extent of medication-related harm is known, potential solutions could be considered and trialed.

1.6.1. Aims

3) To identify problems associated with medication use in New Zealand general practice

    a) To evaluate the extent of medication-related harm arising from prescribing in NZ general practice

    b) To evaluate an automated clinician alert system to see whether there were any inequities in clinician action taken based on patient ethnicity or other demographic factors

4) To explore strategies to improve medication safety in New Zealand general practice

    a) To explore what patients and prescribers would like in a decision support and communication tool

    b) To explore whether a tailored information package for patients can improve

knowledge of NSAIDs and reduce self-reported use of NSAIDs

1.6.2. Objectives

1) To identify problems associated with medication use in New Zealand general practice, two projects were carried out:

    a) A large retrospective records review was undertaken to describe an epidemiology of harm in New Zealand general practice. Sub-analysis of the harms data relating to medication has determined the incidence of medication-related harm arising from general practice prescribing.

    b) Preliminary evaluation of an automated clinician alert system showed that clinicians took actions on the alerts, but there was concern that there was inequity in action taken by ethnicity. Those data have been analysed to determine whether the automated clinician alert system exacerbates ethnic inequity.

2) To explore potential strategies to improve safe medication use in New Zealand general practice, two more projects were undertaken:

    a) Patients and prescribers were interviewed to understand what they would like in a decision support and communication tool.

    b) Findings from the preceding projects were used to develop a tailored information package for patients at higher risk from Non-Steroidal Anti-Inflammatory Drugs (NSAIDs). A randomised control trial (RCT) is required to assess the impact of an information package in improving knowledge of NSAIDs and reducing self-reported use of NSAIDs. To ensure best use of resources for the full RCT, a randomised

feasibility trial was conducted.

1.7. Overview of Methods

This thesis is the work of a general practitioner: general practice is the medical specialty which probably most embodies pragmatism. Pragmatism was introduced to modern philosophy in 1898, borrowed from the work of Immanuel Kant.[163] Pragmatism understands phenomena in relation to their practical consequences, concentrating on "what works" rather than aiming to understand higher truth or reality.[164] Instead, reality is understood through action.[164] Pragmatic responses call for creative ideas, focused problem solving, opportunity to choose and democratic process.[163]

Pragmatic philosophy has found a home in many practical fields such as law, engineering, social work and medicine. By the mid-1990s clinical pragmatism was seen as an important tool in evaluating ethical and moral problems associated with medicine.[165] This approach was subsequently extended to qualitative research methods, described as pragmatic inquiry.[166] Research should be tested for pragmatic validity – research should be both grounded in and useful for clinical practice.[166]

Research aligned with pragmatism obviously uses methods that will best solve the problem at hand. Mixed methods combines quantitative and qualitative methods in a single programme of research.[167] Mixed methods helps answer more complex and nuanced questions than can be answered with quantitative or qualitative methodology alone. It has gained popularity over the past decade, particularly in health research.[168,169] The two main types of mixed method design are described as convergent, where the methods are combined throughout the research, or sequential, where one method informs the next

phase of the research.[169] This thesis uses a sequential mixed methods design to explore patient safety in general practice (Figure 1-2).

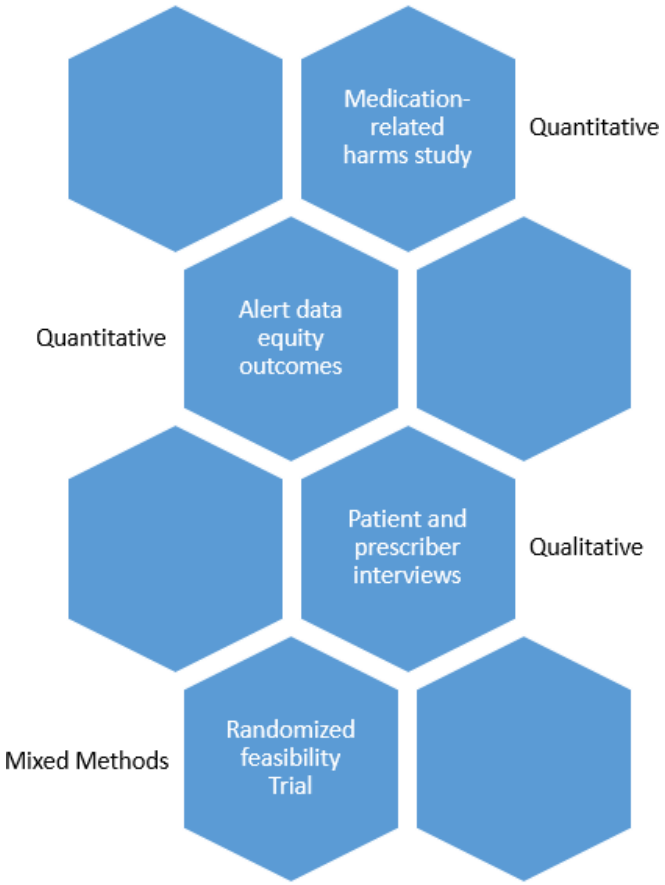

Figure 1-2 Pictorial representation of mixed methods used in this thesis

An example of pragmatism is the evolution of this thesis. The original plan was to build a tailored alert system for this doctoral research project. That work would have used the main learnings from the record review study (described in Study 1), combined with contemporary epidemiological information and medical decision support technology to try to improve medication safety in general practice by averting preventable patient harm. It was to be designed as a communication tool for discussing risks and benefits of medications with patients and their whānau, thereby supporting health education and patient-centered care.

Stakeholder engagement with patients and clinicians was undertaken to ensure the tool was designed to best meet the needs of end-users (Study 3).

In 2018 Conporto Health completed a successful proof-of-concept study for a similar tool, so it was considered unfeasible to continue with the proposed doctoral project. Instead, Conporto Health was willing to collaborate to conduct further patient safety research, leading to two projects. The first project analysed their data to check for health equity issues (Study 2). The second Conporto Health project is closely aligned with my original plan and combines aspects of an alert system with that of patient information and education. Using the knowledge gleaned from the stakeholder interviews a patient education package was developed based on one of the Conporto EDM alerts. A randomised feasibility trial was conducted to determine whether the proposed method is suitable to investigate the impact of providing the information package to patients at risk of renal damage (Study 4).

1.8. Overview of the thesis structure

The thesis takes the form of a series of four linked studies, book-ended by Introduction and Discussion/Conclusion sections (Figure 1-3).

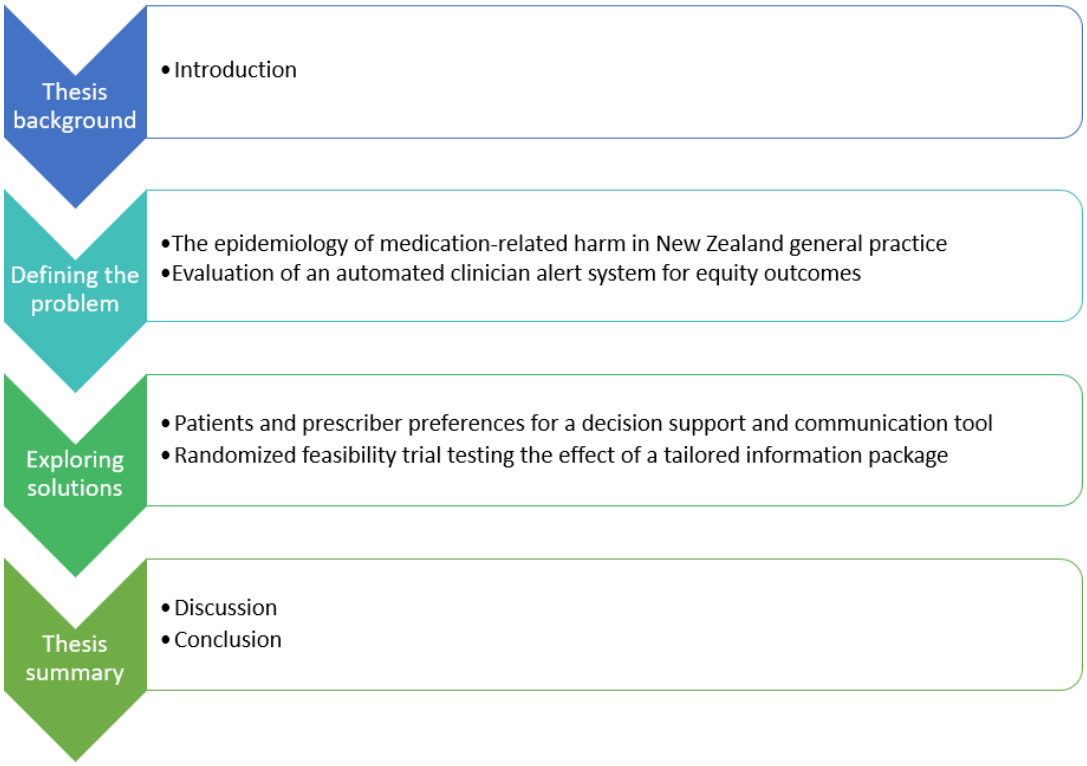

Figure 1-3 Thesis outline

1.9. Summary of Introduction

This chapter has introduced the patient safety movement from international and NZ perspectives, concentrating on medication-related safety issues in general practice. Patient safety terms were defined. The context of NZ general practice was discussed. Strategies to improve patient safety were outlined, as well as barriers to achieving those strategies. Finally, the aims of this thesis were articulated, together with a brief discussion on pragmatism and mixed methods research.

Chapter 2 Medication-related harms in general practice

2.1. Preface

This chapter contains a published original manuscript titled "Medication-related harm in New Zealand general practice: a retrospective records review". This manuscript was published in the British Journal of General Practice in 2021: *Leitch S, Dovey S, Cunningham W, et al. Medication-related harm in New Zealand general practice: a retrospective records review. Br J Gen Pract. 2021;71(709):e626-e633. doi: 10.3399/BJGP.2020.1126.* The manuscript is presented here as published, but has been reformatted to fit the overall thesis style and referencing.

As discussed in the Introduction, while medication safety is considered a priority and has been extensively studied in hospital settings, medication safety in general practice is relatively unexamined. Evaluating patient safety in general practice is difficult due to the intermittent nature of the care provided, and the fact most healthcare is administered off-site (i.e., patients are prescribed medication which they take at home, limiting the capacity to observe and record adverse events). One method of evaluating patient safety in general practice is to review patient records for evidence of patient harm. This method is far from perfect, and has been particularly criticized because results from record review studies are difficult to reproduce.[50,51] However, it is probably the most feasible method we have available to obtain a general (if imperfect) assessment of patient harm in general practice. This chapter explores data from a large record review study for medication-related harm.

The Safety, Harms and Risk Reduction Project (SHARP) is a large retrospective review of NZ

general practice records.[28,113] It aimed to determine the epidemiology of healthcare harm observable in general practice records. SHARP obtained and reviewed the records of over 9000 patients from 44 different practices; at that time the NZ enrolled patient population was 4,092,647 and there were 988 general practices.[170] Reviewers identified 2972 harms of any nature experienced by 1505 patients. The estimated incidence of harm was 123 per 1000 patient-years, and the incidence rate of preventable or potentially preventable harm was 26 harms per 1000 patient-years.[113] This current work is a sub-analysis of those data, examining the medication-related harms that were identified in the SHARP study.

2.1.1. Chapter Aim

To examine the extent of medication-related harm arising from prescribing in NZ general practice – what is the prevalence of harm, and what are the risk factors for experiencing harm?

2.1.2 Candidate Contribution statement

PhD candidate Sharon Leitch was the clinical coordinator for the SHARP study. She recruited the study practices, reviewed general practice records, coded harms, identified medication-related harms arising from general practice prescribing, conducted the statistical analyses, and wrote this manuscript. The full author contributor statement is found at the end of the paper.

2.2 Medication-related harm in New Zealand general practice: a retrospective records review

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2.1 Abstract

2.1.1. Background

The extent of medication-related harm in general practice is unknown.

2.1.2. Aim

To identify and describe all medication-related harm in electronic general practice records. The secondary aim was to investigate factors potentially associated with medication-related harm.

2.1.3. Design and Setting

Retrospective cohort records review study in 44 randomly selected New Zealand general practices for the three years 2011-2013.

2.1.4. Methods

Eight general practitioners reviewed 9076 randomly selected patient records. Medication-related harms were identified when the causal agent was prescribed in general practice. Harms were coded by type, preventability, and severity. The number and proportion of patients who experienced medication-related harm was calculated. Weighted logistic regression was used to identify factors associated with harm.

2.1.5. Results

976/9076 study patients (10.8%) experienced 1,762 medication-related harms over three years. After weighting, the incidence rate of all medication-related harms was 73.9 harms per 1000 patient-years, and the incidence of preventable or potentially preventable

medication-related harms was 15.6 per 1000 patient-years. Most harms were minor (1385/1762, 78.6%), but one in five harms were moderate or severe (373/1762, 21.2%); three patients died. Eighteen study patients were hospitalised; after weighting this correlates to a hospitalisation rate of 1.1 per 1000 patient-years. Increasing age, number of consultations, and number of medications were associated with increased risk of medication-related harm. Cardiovascular medications, antineoplastic and immunomodulatory agents, and anticoagulants caused most harm by frequency and severity.

2.1.6. Conclusion

Medication-related harm in general practice is common. This study adds to the evidence about the risk posed by medication in the real world. Findings can be used to inform decision-making in general practice.

How this fits in

The extent of medication-related harm in general practice is unknown. This retrospective records review found that medication-related harm in general practice iscommon, and is typically minor and arising from standard care. Patients who are older,who have more consultations and who take more medication are at greatest risk of harm. The risk of patient harm increased with age. Patients aged 60–74 years had nearly double the risk of harm compared with the reference group (patients aged 15– 59 years), and patients aged >75 years had triple the risk. This knowledge can inform shared-decision making about treatment options.

2.1.7. Keywords

general practice; New Zealand; patient harm; primary health care; retrospective studies.

2.2. Background

Reducing medication-related harm is a top priority for improving patient safety.[114,171] Primary healthcare settings remain relatively unexamined for patient harm.[172] It is possible patient harm in general practice has been underestimated.[72] Medication-related harm accounts for around 3% of all hospital admissions on average, with higher rates observed in older people.[103-106]

Clinical trials, event reporting, and compensation claims provide a limited perspective on medication-related harm in the real world, producing data not typically generalisable to general practice populations. Population-based records review research can identify harms experienced in the course of routine clinical care, and identify patients at increased risk of harm to improve patient safety.[49]

This study examined medication-related harm in general practice using a subset of data from a nation-wide retrospective cohort review of general practice electronic health records that looked at all harms.[28,170] The primary aim of this paper was to estimate the incidence, preventability and severity of all harms attributable to medication prescribed in general practice in New Zealand. The secondary aim was to investigate factors potentially associated with medication-related harm, including age, sex, ethnicity, social deprivation, number of consultations, number of medications, and general practice size and location.

2.3. Method

2.3.1. Setting

All New Zealand general practices were stratified by size and location.[28,170] Practice size was defined by the number of enrolled patients, divided into tertiles to form three groups consisting of large, medium and small practices. Location was defined as rural or urban based by practice address.[28,170] Practice size and location defined six strata. Twelve practices were randomly selected by from each strata and invited to participate; 44 study practices consented to participate (71.0% of the 62 eligible randomly selected practices with compatible practice software).[170]

2.3.2. Participants

Patients enrolled in recruited practices were randomly selected for participation at the mid-point of the study period; in total 9076 patients were randomly selected (based on prior power calculations).[170] The general practice records of the randomly selected patients for the 3 year study period (1 January 2011 to 31 December 2013, inclusive) were anonymised at time of electronic data extraction. The extracted records contained everything that is normally available in patient records, including demographic data, consultation notes, screening data, laboratory and radiology results, referral letters, alerts, and prescriptions. Secondary care referrals, discharge summaries and clinic letters were available where these had been stored electronically in the record.

Consent and data access were granted by each practice rather than from individual patients.[173] This research was approved by the University of Otago ethics committee, and reviewed by the Ngāi Tahu Research Consultation Committee.

2.3.3. Reviewers

Each patient's file was examined by at least 1 of 8 clinically active GPs with a minimum of 10 years' experience. Reviewers participated in training sessions at the commencement of the study. Feedback from double-reviewed files (*n*=948, 10.4%) was used to further improve reviewer consistency. The range of agreement between pairs of reviewers was 66.7-100.0%; overall kappa = 0.344, *P*<0.001.

2.3.4. Covariates

Patient demographic data including age at 1 July 2012, sex, self-identified ethnicity,[174] and socioeconomic deprivation were obtained. Māori are the indigenous people of New Zealand. Pasifika refers to the people of the Pacific islands (for example, Samoa, Tonga, etc.) who are now living in New Zealand. Participants were sorted into one of five socio- economic categories ranging from 1 (least deprived) to 5 (most deprived) based on their home address and census-derived data for each area meshblock.[175] Information on the number of unique medications prescribed, and number of consultations were also obtained within the specified period. Practice size and location are defined above.

2.3.5. Outcomes

Harm was defined as: "*physical, emotional or financial negative consequences to patients directly arising from health care, beyond the usual consequences of care, and not*

attributable to patients' health conditions".[176] Reviewers identified episodes where patients experienced harm, as documented in their records. Other patient safety measures, such as "near-misses", "safety incidents", "inappropriate prescribing" and "errors," were not recorded unless they resulted in patient harm. Each patient record was recorded in binary terms: harm or no harm.

Harm was rated minor, moderate, severe or death.[28] Short-lived and relatively trivial harms were coded as minor (for example, rashes, vomiting, and inconvenience to patients, such as being given the wrong prescription). Moderate harm was defined as having increased or persistent morbidity (for example, fractures, untreated anaemia, and poor diabetic control). Severe harms included renal failure, pulmonary embolism, myocardial infarction, and morphine overdose. Reviewers used their clinical expertise to assess preventability from five[c] categories.[28,177] Following discussion and consensus these options were aggregated in analysis to "preventable or potentially preventable" (original codes: "preventable and originated in primary care" and "potentially preventable and originated in primary care") and "not preventable" ("not preventable, standard treatment," "not preventable and originated in primary care," "not preventable and originated in secondary care," and "preventable and originated in secondary care OR not preventable and originated in primary care").

Harms were documented in descriptive form, then coded using *Medical Dictionary for Regulatory Activities 18.0* codes.[178] Data extraction is depicted in Figure 2-1. Medications were coded by drug type using the Anatomical Therapeutic Chemical (ATC) classification system.[179]

[c] Erratum. Reviewers used their clinical expertise to assess preventability from six categories.

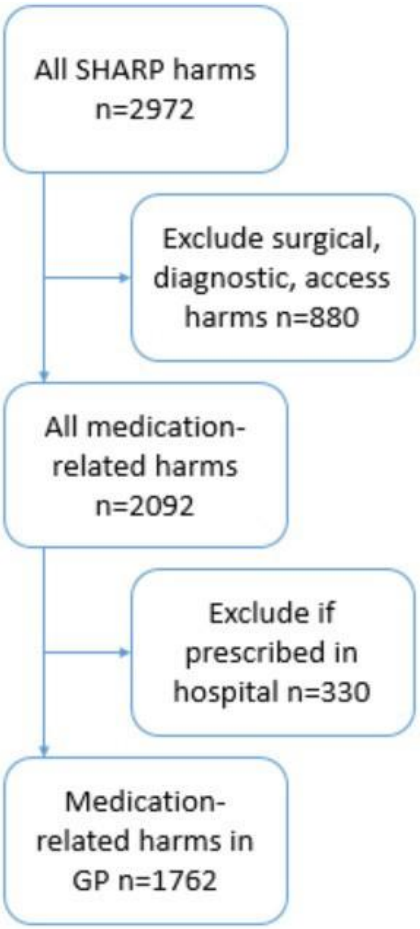

Figure 2-1 Selection of medication-related harms from SHARP data

2.3.6. Statistical Analysis

The number and proportion of medication-related harms was calculated by patient demography (age, sex, ethnicity, and deprivation), clinical information (number of consults and number of unique medications prescribed during the study period), and practice characteristics (practice size and practice location). Incidence rates were calculated as the number of events divided by the total number of person-years of follow-up (for example, 3*9076 years, 3 years per person). In order to obtain an estimate of the incidence of medication-related harm in New Zealand, sampling weights were applied to the incidence rates allowing for the probability of each practice being selected per strata, and each patient being selected per practice. Harms were examined by ATC classification. Individual

medications were examined by rate of prescribing and percentage of patients harmed.

Logistic regression with robust standard error was used to explore associations between medication-related harm and patient demographics, clinical information and practice characteristics. The final model included all covariates listed above. Estimates were then adjusted using appropriate sampling weights.

Stata (version 15.1) was used for all statistical analyses. The Stata svy package was used for applying sample weights. Data were missing for ethnicity (139, 1.5%) and deprivation (894, 9.9%). Complete data analyses were carried out on 8053 patients.

2.4. Results

From 2011-2013 inclusive, 7308 of 9076 (80.5%) patients received 175 657 prescriptions for 846 different medications from their general practices; 1770 (19.5%) patients were not prescribed any medications. Patients were prescribed 0-53 different medications each, (median 4 [IQR 1-9]). Reviewers identified 1762 medication-related harms in 976 (10.8%) patient records over the 3-year study period: 255 different medications were associated with harm. Medication-related harm accounted for 59.0% of all 2972 harms observed in the record review study. After applying weighting, the incidence rate of medication-related harm in New Zealand general practice was 73.9 harms per 1000 patient-years, and the incidence rate of preventable or potentially preventable medication-related harm was 15.6 harms per 1000 patient-years (Table 2-1). Table 2-1 outlines the relationship between medication-related harms, patient demographics, clinical variables (numbers of consultations and medications) and practice characteristics as unweighted data and weighted estimates. Table 2-2 presents the logistic regression models of study variables in relation to medication-

related harm.

Table 2-1 Demographic data of study patients, clinical exposure and practices in relation to medication-related harm related to GP prescribing

		No Harm	Medicine-related harm	No Harm	Medicine-related harm
		Unweighted study data, *n* (%)		Weighted data, *n* (%)[a]	
Total		8100 (89.2)	976 (10.8)	3,737,889 (88.2)	502,404 (11.8)
PATIENTS					
Age	0-4 years	296 (94.6)	17 (5.4)	146,698 (93.0)	11,114 (7.0)
	5-14 years	1283 (97.6)	32 (2.4)	599,128 (96.5)	21,511 (3.5)
	15-59 years	4765 (93.3)	345 (6.8)	2,274,914 (92.1)	195,620 (7.9)
	60-74 years	1217 (80.0)	305 (20.0)	504,945 (76.7)	153,736 (23.3)
	75+ years	539 (66.1)	277 (34.0)	212,204 (63.8)	120,424 (36.2)
Sex	Female	4189 (87.8)	583 (12.2)	1,972,810 (86.9)	298,012(13.1)
	Male	3911 (90.9)	393 (9.1)	1,765,079 (89.6)	204,392 (10.4)
Ethnicity[b]	European	6092 (88.4)	797 (11.6)	2,901,377 (87.1)	428,700 (12.9)
	Māori	1207 (91.0)	119 (9.0)	385,728 (90.2)	42,081 (9.8)
	Pasifika	298 (94.3)	18 (5.7)	102,189 (95.0)	5,322 (5.0)
	Other	384 (94.6)	22 (5.4)	306,709 (93.7)	20,675(6.3)
Deprivation[c]	1	1762 (89.6)	204 (10.4)	1,165,530 (88.5)	150,861(11.5)
	2	1655 (88.9)	207 (11.1)	829,358 (87.4)	119,827 (12.6)
	3	1525 (89.7)	176 (10.3)	663,132 (89.2)	79,880 (10.8)
	4	1202 (88.8)	152 (11.2)	469,926 (87.0)	70,324 (13.0)
	5	1149 (88.5)	150 (11.6)	385,526 (87.1)	57,219 (12.9)
Number of consultations	0-3	2466 (99.7)	8 (0.3)	1,081,613 (99.5)	5,567 (0.5)
	4-12	3096 (95.9)	132 (4.1)	1,476,184 (94.5)	86,466 (5.5)
	13+	2538 (75.2)	836 (24.8)	1,180,091 (74.2)	410,371 (25.8)
Number of medications	0-4	4601 (98.6)	64 (1.4)	2,115,238 (98.0)	43,101 (2.0)
	5-9	2099 (89.1)	257 (10.9)	956,015 (87.3)	139,267 (12.7)
	10+	1400 (68.1)	655 (31.9)	666,636 (67.6)	320,036 (32.4)
PRACTICES					
Practice size	Large	2650 (88.2)	353 (11.8)	2,409,416 (87.0)	358,999 (13.0)
	Medium	2729 (88.6)	351 (11.4)	927,812 (89.6)	107,132 (10.4)
	Small	2721 (90.9)	272 (9.1)	400,661 (91.7)	36,273 (8.3)
Location	Urban	4082 (89.8)	462 (10.2)	3,050,365 (88.0)	416,372 (12.0)
	Rural	4018 (88.7)	514 (11.3)	687,524 (88.9)	86,032 (11.1)

a. Weighting was applied based on the relative probability of each practice being selected per strata, and each person being selected to participate per practice, due to the complex sampling design of the study. Weighting means these results are nationally generalisable to the New Zealand population.

b. Missing data = 139

c. Missing data = 894. Deprivation is based on NZDep index of socioeconomic deprivation, where 1=least deprived, 5=most deprived.[175]

Table 2-2 Logistic regression of study variables in relation to harms arising from medication prescribed in general practice (binary outcome variables medication-related harm: harm or no harm)

	Unadjusted[a]		Adjusted[b]		Adjusted & Weighted[c]	
Variable	**OR (95% CI)**	**P Value**	**OR (95% CI)**	**P value**	**OR (95% CI)**	**P value**
PATIENTS						
Age						
0-4 years	0.79 (0.48-1.31)	0.365	0.56 (0.31-1.00)	0.049	0.75 (0.42-1.33)	0.308
5-14 years	0.34 (0.24-0.50)	<0.001	0.60 (0.41-0.88)	0.010	0.58 (0.31-1.10)	0.095
15-59 years	1 [Reference]	-	1 [Reference]	-	1 [Reference]	-
60-74 years	3.46 (2.93-4.09)	<0.001	1.81 (1.49-2.19)	<0.001	1.98 (1.50-2.61)	<0.001
75+ years	7.10 (5.92-8.51)	<0.001	2.86 (2.30-3.56)	<0.001	3.08 (2.15-4.41)	<0.001
Gender						
Male	1 [Reference]	-	1 [Reference]	-	1 [Reference]	-
Female	1.39 (1.21-1.59)	<0.001	1.07 (0.91-1.26)	0.397	0.98 (0.68-1.43)	0.931
Ethnicity						
European	1 [Reference]	-	1 [Reference]	-	1 [Reference]	-
Māori	0.75 (0.62-0.92)	0.006	1.03 (0.81-1.32)	0.790	1.01 (0.81-1.27)	0.924
Pasifika	0.46 (0.29-0.75)	0.002	0.57 (0.33-0.96)	0.036	0.43 (0.19-0.98)	0.045
Other	0.44 (0.29-0.69)	<0.001	0.86 (0.52-1.42)	0.554	0.68 (0.41-1.15)	0.145
Deprivation[d]						
1	1 [Reference]	-	1 [Reference]	-	1 [Reference]	-
2	1.08 (0.88-1.33)	0.459	1.00 (0.80-1.27)	0.969	1.04 (0.79-1.37)	0.783
3	1.00 (0.81-1.23)	0.977	0.92 (0.72-1.18)	0.528	0.86 (0.58-1.29)	0.457
4	1.09 (0.87-1.36)	0.437	1.05 (0.82-1.36)	0.685	1.15 (0.80-1.65)	0.443
5	1.13 (0.90-1.41)	0.292	1.14 (0.87-1.49)	0.360	1.05 (0.58-1.90)	0.871
Consultations						
0-3	1 [Reference]	-	1 [Reference]	-	1 [Reference]	-
4-12	13.14 (6.43-26.88)	<0.001	6.18 (2.77-13.77)	<0.001	5.38 (1.55-18.67)	0.009
13+	101.54 (50.50-204.16)	<0.001	15.21 (6.74-34.34)	<0.001	11.83 (4.27-32.80)	<0.001
Medications						
0-4	1 [Reference]	-	1 [Reference]	-	1 [Reference]	-
5-9	8.80 (6.66-11.63)	<0.001	3.41 (2.45-4.74)	<0.001	3.05 (2.10-4.44)	<0.001
10+	33.63 (25.84-43.78)	<0.001	7.25 (5.19-10.11)	<0.001	5.71 (3.83-8.50)	<0.001
PRACTICES						
Practice size						
Large	1 [Reference]	-	1 [Reference]	-	1 [Reference]	-
Medium	0.97 (0.83-1.13)	0.662	0.91 (0.75-1.10)	0.336	0.72 (0.46-1.11)	0.134
Small	0.75 (0.64-0.89)	<0.001	0.75 (0.61-0.93)	0.008	0.65 (0.44-0.95)	0.027
Location						
Urban	1 [Reference]	-	1 [Reference]	-	1 [Reference]	-
Rural	1.13 (0.99-1.29)	0.071	0.92 (0.78-1.08)	0.203	0.78 (0.55-1.09)	0.145

a. *Unadjusted: Unweighted univariate logistic regression*
b. *Adjusted: Unweighted multiple logistic regression to adjust for potential confounders – all other variables were considered potential confounders*
c. *Adjusted and Weighted: Multiple logistic regression weighted for the relative probability of each person being selected as a study participant*
d. *Deprivation is based on NZDep index of socioeconomic deprivation, where 1=least deprived, 5=most deprived.*[175]
OR=odds ratio

2.4.1. Patients

Older patients were more likely to experience medication-related harm. In the final model (adjusted and weighted) patients aged 60-74 years had double the odds of experiencing medication-related harm (odds ratio [OR] 1.98, 95% confidence interval [CI] 1.50-2.61), and patients 75 years and older had triple the odds (OR 3.08, 95%CI 2.15- 4.41), compared to patients aged 15-59 years.

Women appeared to be at increased risk of medication-related harms in the unadjusted model, however after adjustment for the other variables there was no difference in risk by sex. The smallest ethnic group was Pasifika ethnicity (*n*=316, 3.5%), which had a lower risk of experiencing harm than Europeans (OR 0.43, 95%CI 0.19-0.98) (Table 2-2). There was no evidence that social deprivation was associated with medication-related harm.

2.4.2. Clinical exposure

Increasing number of consultations and medications were correlated with increased risk of medication-related harm. Compared to patients who had 0-3 consultations over the study period, the odds of experiencing medication-related harm for patients that had 4-12 consultations over the three year study period was 5.38 (95%CI 1.55-18.67) times greater; for patients with >13 consultations over 3 years the odds were 11.83 (95%CI 4.27-32.80) times greater (Table 2-2). Similarly, when compared with patients prescribed 0-4 unique medications in the study period, being prescribed 5-9 medications was associated with an increased OR of medication-related harm of 3.05 (95%CI 2.10-4.44). Being prescribed >10 medications was associated with an increased odds ratio of 5.71 (95%CI 3.83-8.50) (Table 2-2).

2.4.3. Practices

Practice size was associated with risk of medication-related harm, but practice location was not. Patients attending small practices had a lower OR of experiencing medication-related harm compared to patients attending large practices (OR for patients attending small-sized practices 0.65, 95%CI 0.44-0.95; OR for patients attending medium-sized practices 0.72, 95%CI 0.46-1.11) (Table 2-2).

2.4.4. Harms

Most medication-related harm was directly related to the medication (1673/1762, 94.9%), but 5.1% was attributable to indirect causes such as access, communication (for example, asthma deteriorated as patient did not understand fluticasone needed to be taken regularly), or procedures (for example, local pain and swelling following administration of vaccine). Gastroenterological effects were the most common harm type by body system (*n*=387, 22.0%) (Table 2-3). Medication-related harms were mainly of minor severity (*n*=1385, 78.6%) (for example, angiotensin-converting enzyme inhibitor cough). Most medication-related harms were not preventable (*n*=1432, 81.3%) (for example, weight gain with oral contraceptive); the remainder were considered preventable or potentially preventable (*n*=330, 18.7%) (for example, cardiac arrest following co-prescription of medications which increased the QT interval). One in five medication-related harms were moderately severe (*n*=373/1762, 21.1%) (for example, developed type 2 diabetes following long-term course of prednisone) or severe (*n*=44, 2.5%) (for example, ventricular tachycardia and cardiac arrest attributed to amiodarone causing prolongation of the QT interval), and four harms were associated with the death of 3 patients (*n*=4, 0.2%). Eighteen patients were

hospitalised as a result of medication- related harm, representing 0.2% (*n*=18/9076) of all study patients and corresponding to a weighted hospitalisation rate of 1.1 per 1000 patient-years.

Table 2-3 Harm types by system with examples

System *n* (%)	Harm *n= 1762* (% of system)		Examples
General 186 (10.6)	Generally unwell	63 (33.9)	75 year old female felt dizzy and sleepy after taking donepezil. Mild severity, not preventable.
	Fatigue	47 (25.3)	
	Weight change	24 (12.9)	
	Exacerbation of existing condition	20 (10.8)	10 year old male experienced anorexia and poor weight gain on methylphenidate. Mild severity, potentially preventable.
	Other	32 (17.2)	
Gastro-enterology 387 (22.0)	Nausea, vomiting, diarrhoea	213 (55.0)	2 year old female developed diarrhoea after taking amoxycillin. Mild severity, not preventable.
	Constipation	53 (13.7)	
	Dyspepsia	48 (12.4)	81 year old male developed severe constipation from codeine requiring hospitalisation. Severe harm, potentially preventable.
	Bleeding	28 (7.2)	
	Pain	12 (3.1)	
	Other	33 (8.5)	
Cardiology 217 (12.3)	Hypotension	136 (62.7)	93 year old male experienced recurrent falls secondary to hypotension while taking cilazapril, metoprolol, frusemide and isosorbide mononitrate. Moderate severity. Potentially preventable.
	Heart failure	39 (18.0)	
	Arrhythmias	27 (12.4)	
	Other	15 (6.9)	
Neurology 192 (10.9)	Cognition	61 (31.8)	83 year old woman experinced a haemorrhagic cerebrovascular accident after commencing aspirin and clopidogrel, resulting in death. Not preventable.
	Sensory	41 (21.4)	
	Headache	35 (18.2)	
	Balance	32 (16.7)	
	Movement	12 (6.3)	79 year old man developed postural hypotension while taking metoprolol and cilazapril. Fell and developed a subdural haemaotoma, died during hospitalisation for this. Potentially preventable.
	Intracerebral event	11 (5.7)	
Renal 161 (9.1)	Renal	139 (86.3)	69 year old male with severe chronic renal failure died within two weeks of an increased dose of metformin and allopurinol. Death.
	Urology	22 (13.7)	Potentially preventable.
Musculo-skeltal 107 (6.1)	Pain	75 (70.1)	81 year old male experienced repeated episodes of gout while taking bendrofluazide. Mild severity. Potentially preventable.
	Gout	18 (16.8)	
	Bones and joints	14 (13.1)	
Skin 104 (5.9)	Rash	50 (48.1)	8 year old female developed scalp irritation and discomfort after using malathion shampoo. Mild severity, not preventable.
	Itch	23 (22.1)	
	Other	31 (29.8)	
Mental health 101 (5.7)	Mood/affect	66 (65.3)	53 year old male experienced vivid dreams and sleep disturbance while taking varenicline. Mild severity. Not preventable.
	Sleep disturbance	26 (25.7)	43 year old female described as abusing prescribed codeine. Moderate severity. Potentially preventable.
	Addiction	9 (8.9)	
Haematology 81 (4.6)	Haematology	77 (95.1)	49 year old male developed thrombocytopenia while taking carbamazebine. Mild severity. Not preventable.
	Immunology	4 (4.9)	
Endocrine 71 (4.0)	Diabetes related	48 (67.6)	71 year old female taking glipizide and insulin experienced recurrent hypoglycamic episodes. Moderate severity. Potentially preventable.
	Sweating and flushing	10 (14.1)	
	Other	13 (18.3)	
Reproductive health 60 (3.4)	Bleeding	34 (56.7)	51 year old female on dabigatran experienced menorrhagia requiring a blood transfusion. Moderate severity. Not preventable.
	Infection/discharge	18 (30.0)	
	Pregnancy	8 (13.3)	
Respiratory 57 (3.2)	Cough & wheeze	57 (100.0)	71 year old male developed acute pneumonitis while taking amiodarone. Severe harm. Not preventable.
Economic 38 (2.1)	Extra treatment required	38 (100.0)	32 year old male required hospitalisation and time off work for a GI bleed while taking diclofenac and no proton-pump inhibitor. Moderate severity. Potentially preventable.

2.4.5. Medications

Table 2-4 shows harm by ATC classification group. Harms from cardiovascular medications (ATC Group C), predominantly antihypertensives and statins, affected the most patients; 517 patients were harmed of 5965 patients prescribed those medications (8.7%); 2.1% (*n*=11/517) of those harms were severe. Antineoplastic and immunomodulatory agents (ATC Group L) had the highest rate of harm (*n*=21/131, 16.0%) but none of the harms were severe, and these agents were taken by only 1.4% (*n*=131/9076) of patients.

Medication relating to blood and blood forming organs (ATC Group B) were the third most harmful agents affecting 6.0% (*n*=102/1688) of study patients taking those medications, the most harmful being dabigatran (B01AE07), warfarin (B01AA03) and dipyridamole (B01AC07). This group had the highest proportion of severe harms (6.9%, *n*=7/102). Analgesia, antibiotics and asthma medications were among the most commonly prescribed medication types. Of these commonly prescribed medications, diclofenac and amoxicillin with clavulanic acid were associated with the most harm (*n*=27/1016, 2.7% and *n*=21/926, 2.3% respectively).

Table 2-4 Medication-related harm by Anatomical Therapeutic Chemical (ATC) classification group

		Patients harmed/ Patients prescribed unique medicine, *n* (%) *N*=1,433/55,340 (2.6)[a]	Percentage of patients harmed as a proportion of medication-related harm by ATC class 1,433/1,433 (100)
A	**Alimentary tract and metabolism**	124/6,174 (2.0)	8.7
B	**Blood and blood forming organs**	102/1,688 (6.0)	7.1
C	**Cardiovascular system**	517/5,956 (8.7)	36.1
D	**Dermatologicals**	25/6,385 (0.4)	1.7
G	**Genitourinary system and sex hormones**	52/1,482 (3.5)	3.6
H	**Systemic hormonal preparations**	30/1,653 (1.8)	2.1
J	**Anti-infectives for systemic use**	152/10,676 (1.4)	10.6
L	**Antineoplastic and immunomodulating agents**	21/131 (16.0)	1.5
M	**Musculoskeletal system**	91/4,600 (2.0)	6.4
N	**Nervous system**	291/9,178 (3.2)	20.3
P	**Antiparasitics, insecticides and repellents**	4/377 (1.1)	0.3
R	**Respiratory system**	16/5,612 (0.3)	1.1
S	**Sensory organs**	7/1,330 (0.5)	0.5
V	**Various**	1/98 (1.0)	0.1

a. Each unique medicine was counted once per patient. Some patients were prescribed more than one medicine in each ATC code. ATC = Anatomical Therapeutic Chemical.

2.5 Discussion

The incidence rate of medication-related harm in New Zealand general practice after weighting was 73.9 harms per 1000 patient-years; the incidence rate of potentially preventable medication-related harm was 15.6 harms per 1000 patient-years. Most medication-related harms were of minor severity, but three patients died. The hospitalisation rate was 1.1 per 1000 patient-years. Factors strongly associated with medication-related harm were increasing age and clinical exposure. Pasifika ethnicity and attending a small practice were protective. Cardiovascular medications caused the most harm.

2.5.1. Strengths and Limitations

General practice records are a rich data source permitting comprehensive review of medication-related harms.[49] The authors believe this large, detailed, retrospective review of a nationally representative sample of general practice records is likely to provide the closest possible estimate of medication-related harm in the real-world. Harm rates are generalisable to the entire country. There have been few appreciable changes in New Zealand general practice prescribing since the study period, although medication use and polypharmacy have increased slightly.[180,181]

Harm rates presented should be considered a conservative estimate. Only recorded harms are included; it is unknown how many additional harms occurred but were not recorded. The authors assume all patient participants selected at the mid-point of the study period remained enrolled for the three year study period. Medication-related harms were only

included if there was a prescription for the corresponding agent in the electronic medical record. Therefore, harms arising from medications administered or dispensed in general practice without a prescription (for example, some contraceptives, practitioner supply medications[182] etc.) were not included. Additionally, controlled drugs such as morphine and methylphenidate required a hand-written prescription during the study period, but a concurrent electronic prescription may not have been generated. Harms were recorded verbatim – for example, it is not possible to know whether someone would have experienced haematemesis regardless of whether they had been taking diclofenac.

Harm estimates are not easily comparable between studies due to variations in terminology and methodology.[23,26,108] Critics of the record review method point to this and object to low rates of reproducibility.[50,51] However, the records review method is comprehensive and provides unique insight into the patient experience of medication- related harm.[49] Reviewer training and feedback was used to improve reviewer concordance.

2.5.2. Comparison with existing literature

The authors' research found medication-related harm was common, for several reasons. Records were examined for all medication-related harm and not just preventable adverse events or patient-safety incidents; the patient-focused definition of harm is comprehensive; and the authors examined all patient records (not just those considered high risk or identified by a trigger tool). The figures are therefore higher than published figures, although comparisons between these types of studies is difficult. The most comparable systematic review estimated the incidence of preventable adverse drug events as 15 per 1000 person-years,[108] which is equivalent to our incidence rate for preventable or potentially preventable

medication-related harm. Other studies indicate medication-related harm is a substantial problem, but are less comparable with our findings. One meta-analysis found up to 24 patient safety incidents per 100 primary care consultations, with up to 11% of medication-related incidents resulting in patient harm,[107] a literature review found up to 2.3% of deaths followed adverse events attributable to primary care treatment, with up to 42% of serious medication-related harms in primary care considered preventable,[183] while a record review study found 25.7% of preventable harms attributable to medication.[110]

2.5.3. Implications for research and practice

General practice has been considered a relatively safe health care setting. This study found medication-related harm is common in general practice, mostly minor and not preventable, often arising from standard care. However, sometimes harms resulted in severe outcomes including hospitalisation and death; one in four harms were considered at least potentially preventable.[d] These findings reinforce the need for vigilance and care in even routine medication use.

This research adds to the field's knowledge of which patients are at highest risk of medication-related harm; namely, patients who are older, who have more consultations and who take more medications. Identifying these patients may help inform shared decision-making at the time of prescribing and target risk monitoring. Further research is required to determine how best to address and reduce the risk of medication-related harm in the context of routine general-practice prescribing.

Medication-related harm in general practice is common. This study builds on the evidence

[d] Erratum: One in five harms were considered at least potentially preventable.

base about the risk posed by medication in the real world. Findings can be used to inform decision-making in general practice and to target patient safety initiatives towards patients at higher risk of harm.

2.6. Acknowledgements

This research was funded by the Health Research Council of New Zealand (HRC-14-185). Thanks to Ari Samaranyaka, for his contribution to the study design, and to Murray Tilyard in his assistance in establishing the data collecting systems and for his participation as a GP reviewer. This project would not have been possible without the development of data extraction software by Jason Hall and his team at bpac^{nz}. We acknowledge the generous participation of all the study practices who contributed their practice data for this research.

2.7 Declarations

2.7.1. Contributor and guarantor information

Leitch was a clinical coordinator for the study, recruited the study practices, reviewed general practice records, coded harms, conducted statistical analyses, and wrote this manuscript. Leitch is the guarantor for this research and as corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted. Dovey is the Principal Investigator, conceived and undertook the study design, obtained research funding, coded harms, and critically reviewed this manuscript. Cunningham reviewed general practice records, coded harms, and critically reviewed this manuscript. Smith and Zeng provided advice regarding the statistical analyses and critically reviewed this manuscript. Reith, Wallis, Eggleton, McMenamin, Williamson, Lillis, and Tilyard

reviewed general practice records and critically reviewed this manuscript.

2.7.2. Transparency statement

Leitch (the manuscript's guarantor) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as originally planned have been explained. All reasonable requests for data sharing will be considered in light of the existing ethical approval.

2.7.3. License for publication

The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, a worldwide licence to the Publishers and its licensees in perpetuity, in all forms, formats and media (whether known now or created in the future), to i) publish, reproduce, distribute, display and store the Contribution, ii) translate the Contribution into other languages, create adaptations, reprints, include within collections and create summaries, extracts and/or, abstracts of the Contribution, iii) create any other derivative work(s) based on the Contribution, iv) to exploit all subsidiary rights in the Contribution, v) the inclusion of electronic links from the Contribution to third party material where-ever it may be located; and, vi) licence any third party to do any or all of the above.

2.7.4. Competing interests

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: all authors apart from Smith and Zeng had financial support from the Health Research Council of New Zealand for the submitted work;

there are no other relationships or activities that could appear to have influenced the submitted work.

2.8 Chapter Summary

This chapter has examined the extent of medication-related harm arising from prescribing in NZ general practice. Medication harm is relatively common. Most medication-related harms were considered not preventable, but approximately 1 in 5 harms were considered potentially preventable. People at higher risk of harm are those who are older, take more medication, and those who attend their general practice clinic more frequently. These data provide justification for further investigation into medication safety conducted in the rest of this thesis.

Chapter 3 Evaluation of equity in use of an automated clinician alert system

3.1. Preface

The following chapter contains a published original manuscript titled "Medication risk management and health equity in New Zealand general practice: a retrospective cross-sectional study." It was published in the International Journal for Equity in Health in 2021: *Leitch S, Zeng J, Smith A, Stokes T. Medication risk management and health equity in New Zealand general practice: a retrospective cross-sectional study. Int J Equity Health. 2021;20(119):1-8. doi:10.1186/s12939-021-01461-y.* The manuscript is presented here as published, but has been reformatted to fit the overall thesis style and referencing.

As discussed in the Introduction, health equity is a major concern of the NZ health system. Historic injustices and racism have resulted in poor health outcomes for Māori and Pasifika patients. NZ law and health policy recognise the rights of all citizens to fair and equitable treatment. Using the record review method, we found a medication-related harm rate of 73.9 per 1000 patient-years in NZ general practice (Chapter 2). Although no differences were detected in harm rates by ethnicity, these likely still exist. This finding may represent inequitable access to healthcare; however, that study was not powered to detect differences in consultation rates or harm rates by ethnicity.

Various patient safety tools and technologies have been developed to try and prevent or mitigate harm arising from medication for all patients. Conporto Health has developed an Event Detection and Mitigation alert system (Conporto EDM) to alert clinicians when their

patients are at higher risk of experiencing harm from medication.[184] In this system, an automatic electronic record scan is triggered by the patient making an appointment or requesting a prescription, or by presenting to the emergency department (ED), as shown in Figure 3-1. If the scan detects a pre-specified alert, then a warning alert is sent to the clinician, as depicted in Figure 3-2. Conporto EDM was trialled in 2018 in 66 general practices located throughout New Zealand. In their proof-of-concept data review Conporto Health found GPs were not taking action to remedy the potential harm for patients of Māori and Pasifika ethnicity in the same way they were taking action for patients of European ethnicity. To ensure their tool was not worsening inequities in health, Conporto were keen to investigate this preliminary finding further. The aim of this project was therefore to further evaluate data from the Conporto Health automated clinician alert system to see whether there were differences in whether clinicians took action depending on the ethnicity of the patient.

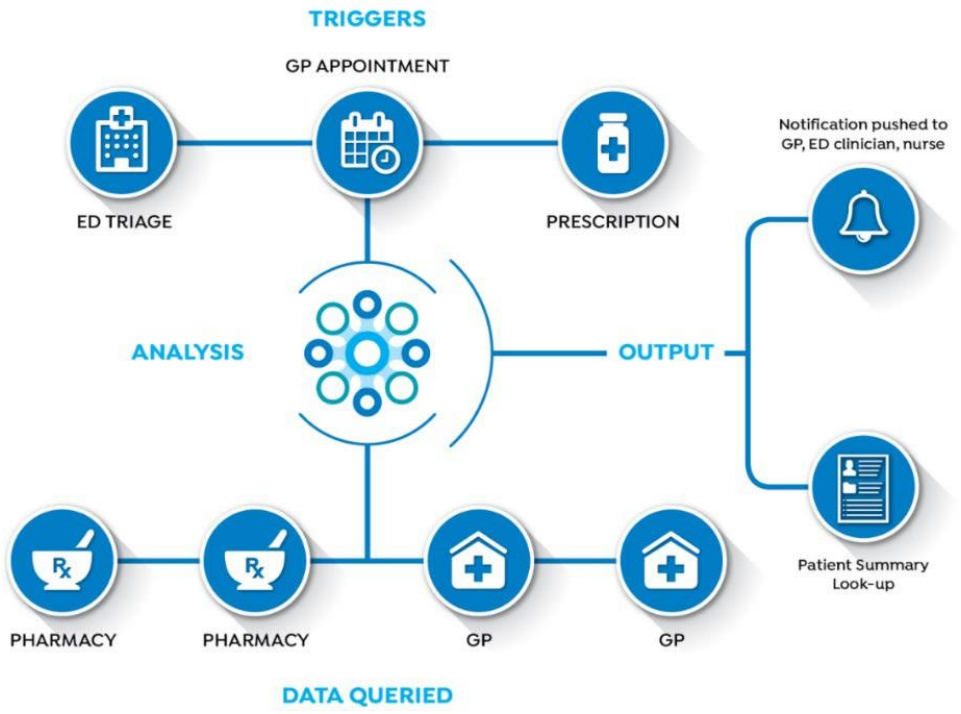

Figure 3-1 Pictorial representation of the Conporto EDM system

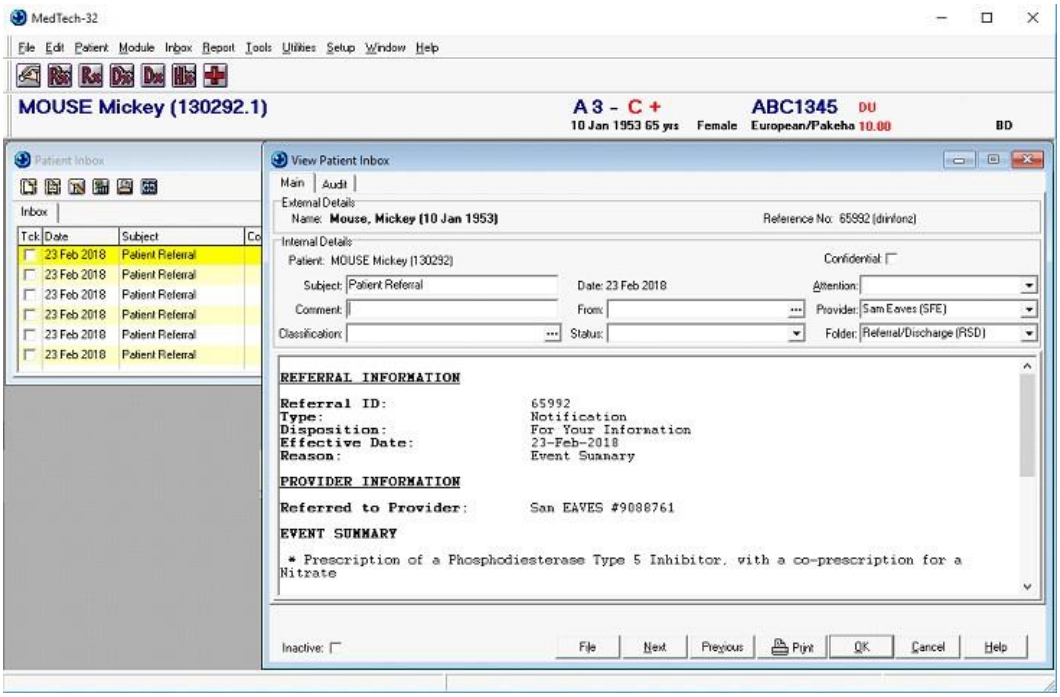

Figure 3-2 Screenshot of the Conporto PMS inbox message event notification

3.1.2. Chapter Aim

To evaluate an automated clinician alert system to see whether there were any inequities in clinician action taken based on patient ethnicity or other demographic factors.

3.1.3. Candidate Contribution statement

PhD candidate Sharon Leitch designed the study, analysed the data and wrote the manuscript. The full author contributor statement is found at the end of the paper.

3.2. Medication risk management and health equity in New Zealand general practice: a retrospective cross-sectional study

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3.3. Abstract

3.3.1. Background

Despite an overt commitment to equity, health inequities are evident throughout Aotearoa New Zealand. A general practice electronic alert system was developed to notify clinicians about their patient's risk of harm due to their pre-existing medical conditions or current medication. We aimed to determine whether there were any disparities in clinician action taken on the alert based on patient ethnicity or other demographic factors.

3.3.2. Methods

Sixty-six New Zealand general practices from throughout New Zealand participated. Data were available for 1611 alerts detected for 1582 patients between 1 Jan 2018 and 1 July 2019. The primary outcome was whether action was taken following an alert or not. Logistic

regression was used to assess if patients of one ethnicity group were more or less likely to have action taken. Potential confounders considered in the analyses include patient age, gender, ethnicity, socio-economic deprivation, number of long term diagnoses and number of long term medications.

3.3.3. Results

No evidence of a difference was found in the odds of having action taken amongst ethnicity groups, however the estimated odds for Māori and Pasifika patients were lower compared to the European group (Māori OR 0.88, 95%CI 0.63-1.22; Pasifika OR 0.88, 95%CI 0.52-1.49). Females had significantly lower odds of having action taken compared to males (OR 0.76, 95%CI 0.59-0.96).

3.3.4. Conclusion

This analysis of data arising from a general practice electronic alert system in New Zealand found clinicians typically took action on those alerts. However, clinicians appear to take less action for women and Māori and Pasifika patients. Use of a targeted alert system has the potential to mitigate risk from medication-related harm. Recognising clinician biases may improve the equitability of health care provision.

3.3.5. Keywords

Ethnicity, equity, decision support, general practice, harm

3.4. Background

Health inequities are defined as differences in health outcomes or risks to health between peoples of different social advantage.[185] Te Tiriti O Waitangi (The Treaty of Waitangi), the founding constitutional document of Aotearoa New Zealand (NZ), upholds the ideals of equity and protection of Māori (the Indigenous people).[79,186,187]

New Zealand provides universal cover for most health services, including hospital-based inpatient and outpatient care.[65] Primary healthcare is delivered in community-based general practices. General practice services and medication for children under the age of 14 years are fully subsidised. However, most other patients co-pay for primary healthcare (typically $13 -$35 USD) and pay a small prescription charge per medication ($3.50 USD). Annual out-of-pocket health spending per capita is $520 USD, accounting for around 12% of New Zealand total health spending.[188] In comparison, the median weekly income is $455 USD; Māori and Pasifika (people living in NZ who identify as Pacific peoples) have lower median weekly incomes than people of other ethnicities.[189]

Systemic racism is widespread in the New Zealand health system.[190] Despite ambitious national goals to "improve, promote and protect the health and wellbeing of New Zealanders,"[191] healthcare inequity persists for Māori and Pasifika.[67] People of Māori and Pasifika ethnicity and people who experience socioeconomic deprivation, have excessively high adverse event rates, including premature mortality, injury, disability, and healthcare-related harms.[15,67,160-162,192] These groups experience under-prescribing of appropriate medications, higher prescribing of inappropriate medications,[193] and higher rates of polypharmacy.[36,62]

Computerised decision support tools can help improve the quality and safety of prescribing by identifying and alerting clinicians to potentially dangerous prescribing actions.[134,140,142,194] Conporto Health Event Detection & Mitigation (Conporto EDM) is an automated alert system that detects whether general practice patients are at high risk of medical harm due to their medical conditions, medications, or for want of mitigating preventative action.[147] Events in this system consist of 10 pre-specified conditions (Table 3-1). The system is triggered by activities such as making an appointment, or a prescription request. Clinicians are informed at the start of each session which of their patients to be seen are at increased risk of harm via secure email, with detailed information sent to the electronic health record "Inbox". The "Inbox" is a portal containing all messages relevant to that patient, including laboratory results, radiology results, correspondence from secondary care, and Conporto EDM alerts. Clinicians have full discretion as to whether they act on the Conporto EDM alerts. Patients are not advised of the alerts unless informed by their clinician. In an attempt to avoid alert fatigue, clinicians are only notified of each triggered Conporto EDM alert once every three months. Therefore, if a Conporto EDM alert is triggered by the patient making an appointment or requesting more medication within three months since the last alert, the clinician will not be notified of those alerts.

Table 3-1 Conporto EDM alerts

Alert	Description
Allopurinol >200mg, eGFR<30	Allopurinol prescribed at a dose of >200mg/day to a patient with chronic renal insufficiency (eGFR <30 mL/min/1.73 m^2)[a]
Macrolide & simvastatin	Prescription for an macrolide antibiotic, with a co-prescription for simvastatin
Bupropion epilepsy	Bupropion (Zyban) prescribed to a patient with epilepsy
Metformin eGFR<30	Metformin prescribed to a patient with renal insufficiency where the eGFR is < 30 mL/min/1.73 m^2
MTX no Folic acid	Prescription of methotrexate, without a co-prescription for folic acid

NSAID eGFR<45	Prescription of a NSAID[b], in a patient with chronic renal insufficiency (eGFR < 45 mL/min/1.73 m^2)
NSAID, Ulcer, no PPI	Prescription of a NSAID, without co-prescription for an proton-pump inhibitor to a patient with a history of peptic ulceration
PDEi & Nitrite	Prescription of a phosphodiesterase type-5 inhibitor, with a co-prescription for a nitrate
Valproate F epilepsy	Prescription of sodium valproate to a female aged 10-59 years with a diagnosis of epilepsy, without history of hysterectomy
Valproate F	Prescription of sodium valproate to a female aged 10-59 years, without history of hysterectomy OR epilepsy

[a]eGFR = estimated glomerular filtration rate, specified here as having been calculated with the Cockcroft-Gault equation

[b]NSAID = Non-steroidal anti-inflammatory drug, e.g. aspirin, ibuprofen, diclofenac, etc.

Preliminary analysis of Conporto EDM data from 1 March – 31 October 2018 was undertaken by Conporto Health.[147] This suggested that although general practitioners did generally take action following an event alert notification, when analysed by individual harm event they appeared less likely to take action for Māori and Pasifika patients.[147] However, important confounders were not adjusted for in those analyses. Also, action rates were evaluated by individual event, even though four of the event groups were too small to make statistical inferences when broken down by ethnicity. We therefore re-examined the association between the actions clinicians took after receiving an event alert and patient ethnicity to determinate robustness of the earlier findings. We did this by grouping all alerts to look at action taken as a whole rather than by individual event, and adjusting for a set of important confounders. The aim of this study is to determine whether there were any disparities in clinician action taken (versus no action) following an alert based on patient ethnicity or other demographic factors.

3.5. Methods

General practices were recruited from all regions of New Zealand, from those participating in the Conporto Health Look-Up programme (an online platform presenting an integrated

summary patient record between healthcare providers). Sixty-six practices signed a consent form to participate in the Conporto EDM proof-of-concept trial. Study participants were patients attending those clinics; individual patient consent was not obtained. Ethical approval for this secondary data review was obtained from the University of Otago Human Ethics Committee (HD19/061). The project was also reviewed by the Ngāi Tahu research consultation committee.

3.5.1. Derivation of study alerts

During the proof-of-concept trial, patient clinical notes were retrospectively reviewed to see whether clinicians took action or not after receiving an alert. The review was undertaken initially by a computer programme which scanned the notes and could determine if action was taken depending on the text, e.g. “stop metformin”; further review was undertaken by a GP and a pharmacist if the results from the computer review were ambiguous.

Conporto Health provided information for all alerts recorded in Conporto EDM between 1 Jan 2018 and 1 July 2019, with patient information retrieved from the general practice records secondary to event data. Figure 3-3 illustrates the steps for the identification of the study alerts. 2499 event alerts were detected within the study period. We excluded 852 alerts where there was no action data recorded; i.e. the medical records had not been reviewed to determine whether action was taken or not. A further 36 events were excluded which had been coded as “false positive” during the proof-of-concept trial, i.e., after checking the medical records, the initial alert was found to be incorrect. Alert data was linked with patient general practice information held by Conporto, extracted from study

general practices using the electronic health record.

Figure 3-3 Derivation of study data

3.5.2. Primary outcome

The primary outcome measure was whether clinicians took action or not after receiving a Conporto EDM alert. All alert types were analysed as one group. Alert consequences were categorised into "action" or "no action taken," as determined by Conporto reviewers during the preliminary analysis period.

3.5.3. Covariates

Ethnicity is self-identified in New Zealand, and people can identify with more than one ethnic group.[101] Prioritised ethnicity was used in concordance with standard New Zealand

health and disability sector use.[101] Patients were categorised to one of the following five categories: European, Māori, Pasifika, Asian and Other. "Other" ethnicity in this dataset includes people of Middle Eastern, Latin American and African ethnicities. Deprivation in New Zealand is assessed by geographical meshblock, by combining census data parameters including income, home ownership, and employment (NZDep13).[195] Patients were assigned to the deprivation groups according to their NZDep13 score, in which deprivation increases by group number. Group 1 (scores 1 and 2) represents the least deprived area; groups 2 (score 3 and 4), 3 (5 and 6), and 4 (7 and 8) are increasingly deprived, while group 5 (9 and 10) represents the most deprived.

In New Zealand, clinicians highlight long-term diagnoses and long-term medications in their patient's electronic health record in order to provide best practice care and facilitate communication between healthcare providers. Typically, long-term diagnoses refer to conditions that the patient receives active treatment for, and serious historic diagnoses. Long-term medications are those which the patient is prescribed regularly (e.g., every three months).

Demographic data (age at the time of the GP appointment, gender, ethnicity and socioeconomic deprivation) and clinical data (number of long-term diagnoses and number of long-term medications) were extracted from the electronic health records. Age, number of long-term diagnoses and long-term medications were treated as categorical variables. Age was divided into three clinically meaningful groups – those aged 1-49 years, 50-74 years and 75 years and older. Numbers of diagnoses and medications are grouped into three clinically meaningful groups; 1-5 long-term diagnoses or long-term medications, 6-10, and 11 or more.

3.5.4. Missing data

Complete data was available for 1235/1611 (76.7%) events. Information on covariates was missing if it was absent in the general practice records. The covariate with the most missing data was long-term medications (301/1611 events, 18.7%), followed by socio- economic deprivation (181/1611, 11.3%) and long-term diagnoses (144/1611, 8.9%).

3.5.5. Statistical analyses

Logistic regression with robust standard error was used to investigate if the actions taken differed across ethnicity groups. Robust standard error allows correlations between the events reported from the same patient. We considered potential confounding by age, gender, socio-economic deprivation, number of long-term diagnoses, and number of long-term prescriptions. Each covariate was initially fitted separately, then with ethnicity. The final model included all covariates.

Unadjusted and adjusted odd ratios along with 95% CI were reported for each covariate. Finally, the EDM alerts were analysed by event type. The number and proportion of notified alerts were reported and of those alerted events, those of actioned events were also reported. Complete-case analysis was used for handling missing data and was performed based on 1235 events. All statistical analyses were performed using Stata software version 15.1.[196]

3.6. Results

Table 3-2 shows events by patient demographic and clinical covariates, by action (whether action was taken or not).

Around half of the alerts resulted in an action (791/1611, 49.1%). Most alerts occurred in

patients aged at least 50 years old (1313/1611, 81.5%) and female (1004/1611, 62.3%). There was no clear pattern of action taken by age group. Females had proportionally less action taken than males (female action taken 458/1004, 45.6%; male 333/607, 54.9%).

NZ European ethnicity constituted 70.6% of the sample (1137/1611), Māori 241 (15.0%), Pasifika 82 (5.1%), Asian 101 (6.3%) and Other 50 (3.1%). Patients of Asian ethnicity were proportionally most likely to have action taken (59/101, 58.4%), and patients of Other ethnicity were least likely to have action taken (17/50, 34.0%). More than 40% of the sample lived in areas of high deprivation (NZDep13 quintile 4 or 5 = 692/1611, 43.0%). There was no clear pattern in the proportion of action taken by deprivation.

The median number of long term diagnoses was 6 (IQR 3-8), and the median number of long-term medication 7 (IQR 4-10). There appeared to be a positive trend towards more action taken with increasing number of both long-term diagnoses and long-term medications.

Table 3-2 Table of events by patient demographic and clinical covariates

Variable	No Action n=820 (50.9%)[a]	Action n=791 (49.1%) [a]	Total n=1611 (100%) [b]
Age in years			
1-49	166 (55.7)	132 (44.3)	298 (18.5)
50-74	351 (47.4)	389 (52.6)	740 (45.9)
75 or more	303 (52.9)	270 (47.1)	573 (35.6)
Missing	0	0	0
Gender			
Male	274 (45.1)	333 (54.9)	607 (37.7)
Female	546 (54.4)	458 (45.6)	1004 (62.3)
Missing	0	0	0
Prioritised Ethnicity			
European	577 (50.8)	560 (49.3)	1137 (70.6)
Māori	128 (53.1)	113 (46.9)	241 (15.0)
Pasifika	40 (48.8)	42 (51.2)	82 (5.1)
Asian	42 (41.6)	59 (58.4)	101 (6.3)
Other	33 (66.0)	17 (34.0)	50 (3.1)
Missing	0	0	0
Deprivation[c]			
1	103 (48.6)	109 (51.4)	212 (13.2)
2	119 (52.2)	109 (47.8)	228 (14.2)
3	159 (53.4)	139 (46.6)	298 (18.5)
4	172 (49.7)	174 (50.3)	346 (21.5)
5	167 (48.3)	179 (51.7)	346 (21.5)
Missing	100 (55.3)	81 (44.8)	181 (11.3)
Long-term diagnoses			
1-5	376 (52.5)	340 (47.5)	716 (44.5)
6-10	287 (49.9)	288 (50.1)	575 (35.7)
11 or more	75 (42.6)	101 (57.4)	176 (10.9)
Missing	82 (56.9)	62 (43.1)	144 (8.9)
Long-term medications			
1-5	281 (53.3)	246 (46.7)	527 (32.7)
6-10	244 (47.0)	275 (53.0)	519 (32.2)
11 or more	112 (42.4)	152 (57.6)	264 (16.4)
Missing	183 (60.8)	118 (39.2)	301 (18.7)

[a] Action Columns show number, row percentage

[b] Total Column shows number, column percentage for each section

[c] Deprivation: 1 represents the least socioeconomically deprived, 5 the most deprived.

Table 3-3 shows that the adjusted odds of having action taken for Māori patients was 0.88 (95%CI 0.63-1.22) times that of European patients. Similarly, Pasifika ethnicity was associated with a reduced adjusted odds of receiving actions (OR=0.88, 95%CI 0.52-1.49) compared to Europeans. Although the estimated odds suggest that Māori and Pasifika patients were less likely to be treated, the results are not statistically significant. In addition, patients of Asian ethnicity had increased odds of having action taken (OR 1.39, 95% CI 0.86-2.23), however the association was not statistically significant.

Women had reduced odds of having action taken compared to men in both the unadjusted and adjusted models. After adjusting for confounding, the odds ratio for women having action taken for an alert was 0.76 (95%CI 0.59-0.96). There was no association found between action taken and age, social deprivation, number of long-term diagnoses, or number of long-term medications.

Table 3-3 The unadjusted and adjusted odds ratios of action for all events taken, by patient characteristics and clinical covariates

Variable	No Action n=820 (50.9%)[a]	Action n=791 (49.1%) [a]	Total n=1611 (100%) [b]
Age in years			
1-49	166 (55.7)	132 (44.3)	298 (18.5)
50-74	351 (47.4)	389 (52.6)	740 (45.9)
75 or more	303 (52.9)	270 (47.1)	573 (35.6)
Missing	0	0	0
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Missing	0	0	0
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European	577 (50.8)	560 (49.3)	1137 (70.6)
Māori	128 (53.1)	113 (46.9)	241 (15.0)
Pasifika	40 (48.8)	42 (51.2)	82 (5.1)
Asian	42 (41.6)	59 (58.4)	101 (6.3)
Other	33 (66.0)	17 (34.0)	50 (3.1)
Missing	0	0	0
Deprivation[c]			
1	103 (48.6)	109 (51.4)	212 (13.2)
2	119 (52.2)	109 (47.8)	228 (14.2)
3	159 (53.4)	139 (46.6)	298 (18.5)
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5	167 (48.3)	179 (51.7)	346 (21.5)
Missing	100 (55.3)	81 (44.8)	181 (11.3)
Long-term diagnoses			
1-5	376 (52.5)	340 (47.5)	716 (44.5)
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Missing	82 (56.9)	62 (43.1)	144 (8.9)
Long-term medications			
1-5	281 (53.3)	246 (46.7)	527 (32.7)
6-10	244 (47.0)	275 (53.0)	519 (32.2)
11 or more	112 (42.4)	152 (57.6)	264 (16.4)
Missing	183 (60.8)	118 (39.2)	301 (18.7)

[a] Action Columns show number, row percentage

[b] Total Column shows number, column percentage for each section

[c] Deprivation: 1 represents the least socioeconomically deprived, 5 the most deprived.

Table 3-4 shows that just under half of the events were actioned overall (791/1611, 49.1%). The majority of events were notified (1358/1611, 84.3%). Of those notified, 58.2% (791/1358) were actioned. The most common event detected was co-prescription of a macrolide antibiotic and simvastatin. This accounted for more than one quarter of events (425/1611, 26.4%). The least common event was a prescription for buproprion in a patient diagnosed with epilepsy (4/1611, 0.3%). Excluding buproprion, notification rates ranged from 98.2% (160/163 females of childbearing age prescribed sodium valporate for epilepsy) to 55.8% (24/43 patients with low renal function who were prescribed a high dose of allopurinol). Clinicians proportionally took the most action for patients who were taking methotrexate but not folic acid (98/155, 63.2%), and (excluding buproprion) the least action for females of childbearing age taking sodium valproate for epilepsy (48/163, 29.5%). Individual event action rates (excluding buproprion) following notification ranged from 30.0% - 87.5%.

Table 3-4 All Conporto EDM Alerts

Alert	**N (% of all events)**	**Notified (% of event)**	**Actioned (% of notified)**
Macrolide & Simvastatin	425 (26.4)	363 (85.4)	239 (65.8)
NSAID eGFR<45	372 (23.1)	302 (81.2)	165 (54.6)
Meformin eGFR<30	187 (11.6)	161 (86.1)	113 (70.2)
Valproate F	178 (11.1)	157 (88.2)	63 (40.1)
Valproate F epilepsy	163 (10.1)	160 (98.2)	48 (30.0)
MTX no folic acid	155 (9.6)	118 (76.1)	98 (83.1)
PDEi & Nitrite	51 (3.2)	44 (86.3)	29 (65.9)
Allopurinol >200mg eGFR<30	43 (2.7)	24 (55.8)	21 (87.5)
NSAID, ulcer, no PPI	33 (2.1)	25 (75.8)	15 (60.0)
Buproprion epilepsy	4 (0.3)	4 (100)	0 (0)

3.7. Discussion

3.7.1. Summary of findings

We found no evidence supporting the assertion that Māori or Pasifika ethnicity groups are associated with lower odds of clinicians taking action after an alert based on the reported confidence intervals. However, the estimated odds ratios do suggest that Māori or Pasifika ethnicity is associated with lower odds of clinicians taking action after an alert. Women had nearly double the number of alerts compared to men, which is consistent with the fact women see their GPs more frequently than men, even after excluding consultations relating to gynaecological and obstetric conditions.[197] Our study suggests that females were less likely to have action taken compared to males following an alert. Women have a long history of experiencing inequitable health care compared to men, such as receiving less pain relief for similar levels of acute and chronic pain.[198,199] This may be attributable to the status of women in society; addressing gender equality is considered an important factor in improving women's health.[200]

3.7.2. Strengths and limitations

This paper provides a snapshot of high-needs general practice patients in New Zealand, as well as some of the risks they are exposed to while receiving routine healthcare. This study had a wide geographical spread of patients, and an ethnic distribution profile similar to the New Zealand population, although the study had a lower proportion of Asian patients and a higher proportion of Other ethnicities.[201] A weakness of this study is that it could be underpowered to detect differences by ethnicity. Also, one quarter of participants had at

least one missing covariate, and thus were not included in the analysis.

3.7.3. Comparison with existing literature

The underlying premise of this work was a rich literature demonstrating increased risk of harm and unfair treatment of people based on ethnicity. This is well documented for Māori and Pasifika patients.[67,190] Migrants and people who don't speak English face additional challenges in a healthcare setting due to cultural and language barriers.[202,203] In addition, preliminary review of these data led us to anticipate differences in clinician action based on ethnicity.

Our findings suggest patient gender is associated with whether general practice clinicians take action after receiving an alert. It is possible that patient ethnicity also has some effect, although our results are not statistically significant. While other factors may be at play, implicit associations of gender and ethnicity can play a role in medical judgement and result in biased provision of care.[204-207]

3.7.4. Implications for health policy

As the proportion of older patients increases in New Zealand general practice, so too do their numbers of long-term conditions and long-term medications.[62,181] The burden of multimorbidity is known to be particularly high for Māori and Pasifika patients.[61] These factors add to the complexity of general practice consultations.[60] Targeted alert systems can help busy general practitioners identify patients at greatest risk of experiencing medication-related harm, and take actions to mitigate those risks.[142,208] Clinicians in this study took action following receipt of targeted event alerts more often than not. Promoting use of such a system has the potential to reduce medication-related harm in general practice.

Inequitable care is evident throughout the New Zealand health system.[67,187] The causes for this are multifactorial; no doubt racism and sexism contribute to health inequities, adverse patient experiences and negative health outcomes.[209,210] While addressing these issues at a system level is important,[67] this paper focused on the action of individual clinicians. Training clinicians to speak up against racism and sexism, as well as recognise their own implicit biases, may help reduce inequities based on those characteristics.[204,211-213]

3.8. Conclusion

This analysis of data arising from a general practice electronic alert system in New Zealand assessed whether clinicians took action on those alerts. Clinicians typically did take action. Our study has found no evidence to support the assertion that Māori and Pasifika ethnicity are associated with lower odds of having action taken on an alert, although the adjusted odds ratios suggest these ethnicity groups are associated with a lower odds, and therefore future studies would benefit from larger samples to investigate this research question further. Female sex is also associated with lower odds of having action taken. Recognising clinician biases may improve the equitability of health care provision.

3.9. List of abbreviations

Conporto EDM – Conporto Health Event Detection & Mitigation system

GP – general practitioner

NZ – New Zealand

EHR – Electronic Health Record

3.10. Declarations

3.10.1. Ethics approval and consent to participate

Consent and data access were granted by Conporto Health, which has an existing research agreement with a network of New Zealand general practices. This research was approved by the University of Otago ethics committee (HD19/061), and reviewed by the Ngāi Tahu Research Consultation Committee.

3.10.2. Consent for publication

Not applicable

3.10.3. Availability of data and materials

The online version contains the anonymised dataset as a supplementary file.

3.10.4. Competing interests

The authors declare that they have no competing interests.

3.10.5. Funding

This work was completed as part of SL's Clinical Research Training Fellowship funded by the Health Research Council of New Zealand (HRC 18-031). The Health Research Council had no input in the design of the study and collection, analysis, and interpretation of data, nor in writing the manuscript.

3.10.6. Authors' contributions

SL designed the study, analysed the data and wrote the manuscript. JZ provided guidance regarding the statistical analyses and critically reviewed the manuscript. AS and TS critically reviewed the study design and manuscript.

3.10.7 Acknowledgements

This project would not have been possible without the support of Conporto Health Ltd who engaged in discussions around patient safety stimulating this research, and provided their data for analysis.

3.10.8 Authors' information

SL is a PhD Candidate; this work has been undertaken as part of her PhD thesis. TS, AS and JZ are her PhD Supervisors.

3.11. Chapter Summary

This chapter has explored an existing data set to determine whether there were inequities by ethnicity in the action taken by GPs following an a patient alert. It is an example of the type of work that could be routinely undertaken to evaluate equity of health service provision. This chapter has highlighted the inherent systemic and clinician biases present in NZ health care delivery - taking a patient-centered approach may help address these biases. Chapter 4 takes this approach; patients and GPs are interviewed about a proposed tool to reduce harm from medication.

Chapter 4 Patient and prescriber perspectives on a decision support and communication tool

4.1. Preface

The following chapter contains a published original manuscript titled "The views of doctors and patients on a proposed risk assessment and communication tool: a qualitative study using Normalisation Process theory." It was published in Implementation Science Communications in 2020: *Leitch S, Smith A, Crengle S, Stokes T. The views of doctors and patients on a proposed risk assessment and communication tool: a qualitative study using Normalisation Process theory. Implement Sci Commun. 2021;2(16)1-12. doi: 10.1186/s43058-021-00120-1.* The manuscript is presented here as published, but has been reformatted to fit the overall thesis style and referencing.

As discussed in the first half of this thesis, medication use in NZ general practice is associated with patient harm. Chapter 2 described an epidemiology of medication-related harm, finding an incidence of 73.9 harms per 1000 patient-years. Chapter 3 presented analysis of an alert system that aimed to mitigate that medication-related harm, which suggested the effectiveness of alerts may be affected by clinician biases. The second half of this thesis is informed by those data, and suggests strategies to reduce medication- related harm.

Systems theory as applied to health care delivery was discussed in the Introduction, in particular the Systems Engineering Initiative for Patient Safety (SEIPS) model was introduced as an example of a human factors/ergonomics (HFE) framework for better understanding

work systems and related interactions and outcomes in healthcare. Systems theory is useful for analysing complex systems to help understand failure and success in the context of the whole system. Implementation science is related to systems theory, but has a stronger focus on the methods used to promote the uptake of evidence-based practices into routine use to improve the efficacy and quality of healthcare services. One implementation science theory is Normalisation Process Theory (NPT), which was chosen for use in this project as it was a good fit and has been widely used in this area – further details about this theoretical framework are elaborated on below.

The Introduction also discussed how shared decision making can improve medication-safety, but poor health literacy is a common limiting factor to participating in shared decision-making. One potential solution is to provide patients with specific, tailored information about their medications at an appropriate health-literacy level. Therefore development of a risk assessment and communication tool was planned. In preparation, the work presented in this chapter was undertaken. It aimed to explore what patients and prescribers want in a decision support and communication tool. Ultimately, the tool was not developed, as a similar tool was released onto the NZ market in 2018 (Conporto Health EDM), and it was considered unfeasible to progress in developing the proposed tool. Nonetheless, the information contained in this chapter is useful to understand what the key stakeholders in a clinical consultation want from such a tool.

4.1.1. Chapter Aim

To explore what patients and prescribers would like in a decision support and communication tool

4.1.2. Candidate contributions

PhD candidate Sharon Leitch conceived and designed the study, undertook the interviews, analysed the data and drafted the manuscript with support of her supervisors and co-authors. The full author contributor statement is found at the end of the paper.

4.2. The views of New Zealand general practitioners and patients on a proposed risk assessment and communication tool: a qualitative study using Normalisation Process Theory

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4.3. Abstract

4.3.1. Background

Communicating risks of medication harm and obtaining informed consent is difficult due to structural barriers, language and cultural practices, bias, and a lack of resources appropriately tailored for the health literacy of most patients. A decision support tool was proposed to alert prescribers of risk and provide tailored information for patients to facilitate informed decision-making with patients and their whānau (family) around medication use. Patient and prescriber co-design was used to ensure the tool was designed to best meet the needs of end-users and avoid increasing health inequity. This paper describes the first stage of the co-design process.

4.3.2. Method

Normalisation Process Theory (NPT) was used to prospectively evaluate the tool. Semi-structured interviews were held with fifteen patients (five Māori, five Pasifika and five NZ European) and nine general practitioners (two Māori and seven European).

4.3.3. Results

Three themes were identified, which related to the three NPT concepts most relevant to developing the tool. Theme 1 (coherence: meaning and sense making by participants) explored participants' understanding of prescribing safety, medication harm and risk, which is based on experience. Patients want as much information as possible about their medications and risk, but doctors find it difficult to communicate that information.

Theme 2 related to the NPT concept of cognitive participation (commitment and engagement by participants) explored what participants thought about a prescribing decision support tool. Participants were cautiously optimistic, but worried about potential harm arising from its use. They also identified requirements for the tool and features to avoid. Theme 3 describes the collective action required for successful implementation of the tool; namely, culturally safe and trustworthy doctor-patient relationships.

4.3.4. Conclusion

Patients and general practitioners provided different perspectives when prospectively evaluating the proposed risk assessment and communication tool. This co-design research identified important pre-requisites for the tool and features to avoid, and novel ideas for the proposed tool. Overall participants supported the development of the proposed risk assessment and communication tool, but identified the important role that doctor-patient relationships would play to ensure successful implementation. Use of Māori and Pacific languages in the proposed tool may enhance engagement and understanding.

4.3.5. Keywords

Normalisation Process Theory, Communication, Risk, Medication Harm, General Practice, Equity

4.4. Contributions to the literature

- A novel electronic decision support tool for use in New Zealand general practice aims to assess patient risk of medication harm, and improve risk communication and shared decision-making.
- Patient and general practitioner co-design aims to anticipate implementation issues, improve the tool's utility, and mitigate health inequities arising from its use.
- This paper describes the use of Normalisation Process Theory as a way to aid the prospective evaluation of the proposed tool by general practitioners and patients.
- Normalisation Process Theory enabled exploration of the concepts of safe prescribing, medical autonomy, and cultural safety in the context of New Zealand general practice.

4.5. Background

Prescribing medication presents a tension between risks and benefits. Prescribers have a legal and moral obligation to ensure patients are fully informed about those risks and benefits.[148,149,214,215] Obtaining truly informed consent can be challenging due to structural barriers, language, differing cultural practices and expectations, bias, and a lack of resources appropriately tailored for the health literacy of most patients.[159,192,216]

Health inequities are potentially avoidable differences in health between peoples of

different social groups.[185] The founding document of Aotearoa New Zealand (NZ), is Te Tiriti O Waitangi (The Treaty of Waitangi), which, among other things, enshrines the concepts of equity and protection of Māori (the Indigenous people).[79,186,187] Health inequity in NZ arises from the corrosive effects of colonisation and racism.[192,217-220] Aspirational goals to "improve, promote and protect the health and wellbeing of New Zealanders,"[191] have done little to address the inequity experienced by Māori and Pasifika (people living in NZ who identify as Pacific peoples, including Samoan, Cook Islands Māori, Tongan, etc.).[67]

Māori, Pasifika, and people who experience socioeconomic deprivation bear a greater burden of disease and have worse health outcomes across a broad range of health conditions in NZ, including birth outcomes, rheumatic fever, meningococcal disease, long term conditions, multimorbidity and cancer.[61,221-226] These populations experience disproportionately high adverse event rates, including premature mortality, injury, disability, and harms arising from healthcare.[15,67,160-162,192] They paradoxically experience both under-prescribing of appropriate medications, higher prescribing of inappropriate medications,[193] and higher rates of polypharmacy.[36,62]

Primary health services provide the majority of healthcare in NZ,[187] typically requiring out-of-pocket co-payments, as do prescription medications.[227] The 2018-19 NZ Health Survey found that similar proportions of Māori, Pasifika and NZ European had attended a general practitioner (GP) in the previous 12 months and that the mean number of visits was higher in Māori (age sex standardised rate ratio 1.22).[228] However, a higher proportion of the Māori and Pasifika populations reported unmet need for primary health care due to the cost of primary health care over the same period (21.9% of Māori and 19.4% of Pasifika vs 12.7% of European/Other).[228] A higher proportion of Māori and Pasifika (11.8% of Māori and 14.0% of

Pasifika vs. 4.2% of European/Other) reported not having a prescription filled because of the cost.[228] Overrepresentation of Māori and Pasifika in lower socio-economic groups compounds inequity.[35,217]

Health literacy is the ability to obtain, process and understand health information in order to make informed and appropriate health-related decisions.[156] Low levels of health literacy are associated with worse healthcare outcomes.[157] New Zealanders typically have low levels of health literacy – over half of adults surveyed had skills "insufficient to cope with the health literacy demands they typically face."[159] The proportion of the Māori population with low health literacy levels is higher with 80% of Māori men and about 75% of Māori women experiencing low levels of health literacy.[159] While policy and public programmes may address health literacy at the national level, clinicians are responsible for communicating health information so patients can understand, whatever their health literacy level.[229]

Decision support tools can improve patient knowledge of their options and expectations of outcomes, support patient participation in shared decision making, and improve communication between patients and clinicians.[158] Decision support tools available in NZ primary care either focus solely on medication interactions or algorithms for specific medication use. A novel tool which integrates these concepts would potentially address some of the above issues. The development of such a tool was proposed. The tool would alert prescribers to medication risk based on potential interactions and patient factors (e.g., renal function), and provide both clinician decision support and patient information, thus facilitating communication and supporting informed decision-making. The aim of this study is to determine what potential users of the tool (patients and GPs) think about the proposed tool. It is hoped this process will help identify unforeseen issues, such design features that

could exacerbate health inequities or be culturally unsafe.[230]

4.5.1. Theoretical Framework

This research utilises an implementation science approach. Implementation science has the capacity to increase the impact of health disparity research and mitigate inequities due to its broad focus on all aspects of implementation, from health policy to bedside.[231-233] Further, implementation science theories can provide a framework for the collection and analysis of data and help explain the findings.[234] We have chosen to use one particular implementation science theory: Normalisation Process Theory (NPT). NPT bridges the translational gap between research evidence and practical implementation, and is comprehensive, flexible and has a strong focus on participatory co-design.[234-237] NPT has been used for research involving ethnic minority populations and to explore issues of equity. [238-241] NPT provides a useful framework for researchers to anticipate implementation issues while designing a complex intervention and its evaluation.[235-237,242] Early use of NPT was initially in eHealth interventions, however its use has spread well beyond this field.[235-237]

Table 4-1 Normalisation process theory (NPT) concepts in developing an e-tool

NPT Concept[243]	Example interview questions*
Coherence Is the intervention meaningful for participants? Establish shared definitions and understanding of both the problem and the potential intervention	**Patient questions:** What does harm from medicine mean to you? What does risk from medicine harm mean? When do you think it's important to know about your risk from medication? Do you think it's important to discuss medication risk with your GP? **GP questions:** What prompts you to consider assessing a patient's risk from their medication? How confident do you feel explaining medication risk to patients?
Cognitive Participation Do participants think the intervention is a good idea? Establish whether patients and doctors are committed to engage with this tool	**Patient questions:** Do you think the proposed MedKōrero tool, to assess risk and improve communication about that risk, will help you/your whanau make decisions about treatment? What kind of impact would a tool like this have for you/your whanau when you are deciding on a treatment option? **GP questions:** Do you think the proposed MedKōrero tool, to assess risk and communicate that risk to patients, will promote shared decision making? Would it be helpful to your day-to-day work?
Collective Action What work needs to be done to implement this new intervention? Ascertain the likely work participants will need to do to in relation to the tool, in order to learn what features the tool requires in order to minimise additional work.	**Patient questions:** What would promote its use? What would be a barrier to its use? **GP questions:** What kind of impact would a tool like this have in your clinical setting? What would promote its use? What would be a barrier to its use?
Reflexive Monitoring Ascertain the likely impact of the tool, in order to develop the tool to enhance positive impact and minimise negative impact.	**Patients and GPs:** Can you think of potential system-wide effects of using this tool? What would be the intended and unintended consequences

**Appendix 2 contains the complete interview guide*

NPT considers implementation as a social process which requires ongoing work by the parties involved and is divided into four domains, outlined in Table 4-1: Coherence, Cognitive Participation, Collective Action and Reflexive Monitoring. Minimising the amount of work required to use the tool and any potential disruption to workflow will help ensure that the tool is actually used.[129]

4.6. Method

The consolidated criteria for reporting qualitative research guidelines (COREQ) were used to prepare this article (see Appendix 1 for full methodological details).[244]

Stakeholder co-design was planned to ensure the tool was designed to best meet the needs of end-users.[245] Semi-structured interviews were conducted using a topic guide (Appendix 2), which was informed by the domains of NPT most relevant to prospectively evaluating a tool: Coherence, Cognitive Participation and Collective Action. Participants were essentially co-opted to participate in the cognitive work of developing ideas around the tool during the course of the interview. Participants were advised of the broad overview of the tool in the advertising material, the participant information sheet, the consent form, and verbally at the start of the interview as follows. “We want to develop and trial a tool, to alert primary care prescribers when patients are at increased risk of harm from medication. We hope this tool will facilitate communication about medication risks and empower shared decision-making about medication use between patients and prescribers. We want to talk to patients and prescribers about their opinions about a tool like this, to help develop a tool that is going to best help both patients and prescribers.” No prototype was presented as it was considered that may overly influence participants’ comments.

The prescriber (GP) interview framework was pilot tested with a GP prescriber by SL and TS observing, who then provided feedback on further iterations of the topic guide. No changes were made as a result of the pilot interview and it was not included in the analysis. The topic guides were used flexibly to allow participants to construct their accounts in their own terms.

4.6.1. Recruitment

A purposive sampling approach was taken for recruitment of both doctors and patients, with the aim of recruiting ethnically diverse samples, particularly of patients. Participants were recruited by personal contact and Facebook group pages. The study team anticipated that we would not need any more than 15 patient or GP interviews to reach data saturation in each group. See Appendix 1 for further details of the recruitment strategy.

SL was identified as a GP and a PhD candidate and recruited all participants. Participants received information about the study and signed a consent form prior to their interview.

4.6.2. Data collection

SL interviewed all participants once, either in person, by phone or videoconference between 8 April and 2 July, 2019. Face-to-face interviews were conducted in a place of the participants choosing; either in a University office, a café, the patient's workplace or home. All interviews were conducted in English. Interviews were recorded and transcribed. Interview field notes were taken during phone and videoconference interviews only. One prescriber phone interview could not be recorded; this interview was written up from detailed interview notes. Two prescriber participants supplemented their interview by emailing further information or background documents after the interview.

Nine doctor and 15 patient interviews were undertaken. Data was transcribed and preliminary analysis occurred concurrently with the interviewing process. Data saturation was reached before the conclusion of these interviews with no new ideas being discussed by participants.

4.6.3. Data analysis

A deductive thematic analysis was conducted using the framework method.[246] Interviews were coded by SL, assisted by NVivo 11 software, into the three relevant NPT domains. Interpretation of the data was an iterative process which was led by SL, with review of the codes, subcategories, categories and themes by TS.

4.7. Results

Fifteen patients (five Māori, five Pasifika and five European patients) and nine doctors (two Māori and seven European general practitioners) were interviewed (Table 4-2).

Table 4-2 Demographic details of study participants

		Patients	**Doctors**
Gender	Male	4	6
	Female	11	3
Age	<50	8	4
	≥50	7	5
Ethnicity	European	5	7
	Māori	5	2
	Pasifika	5	0
Location	Rural	0	2
	Urban	15	7

Figure 4-1 outlines the Normalisation Process Theory (NPT) framework together with the categories and subcategories developed from the interview data, and how the coding frame relates to the study themes. Illustrative participant quotes are presented.

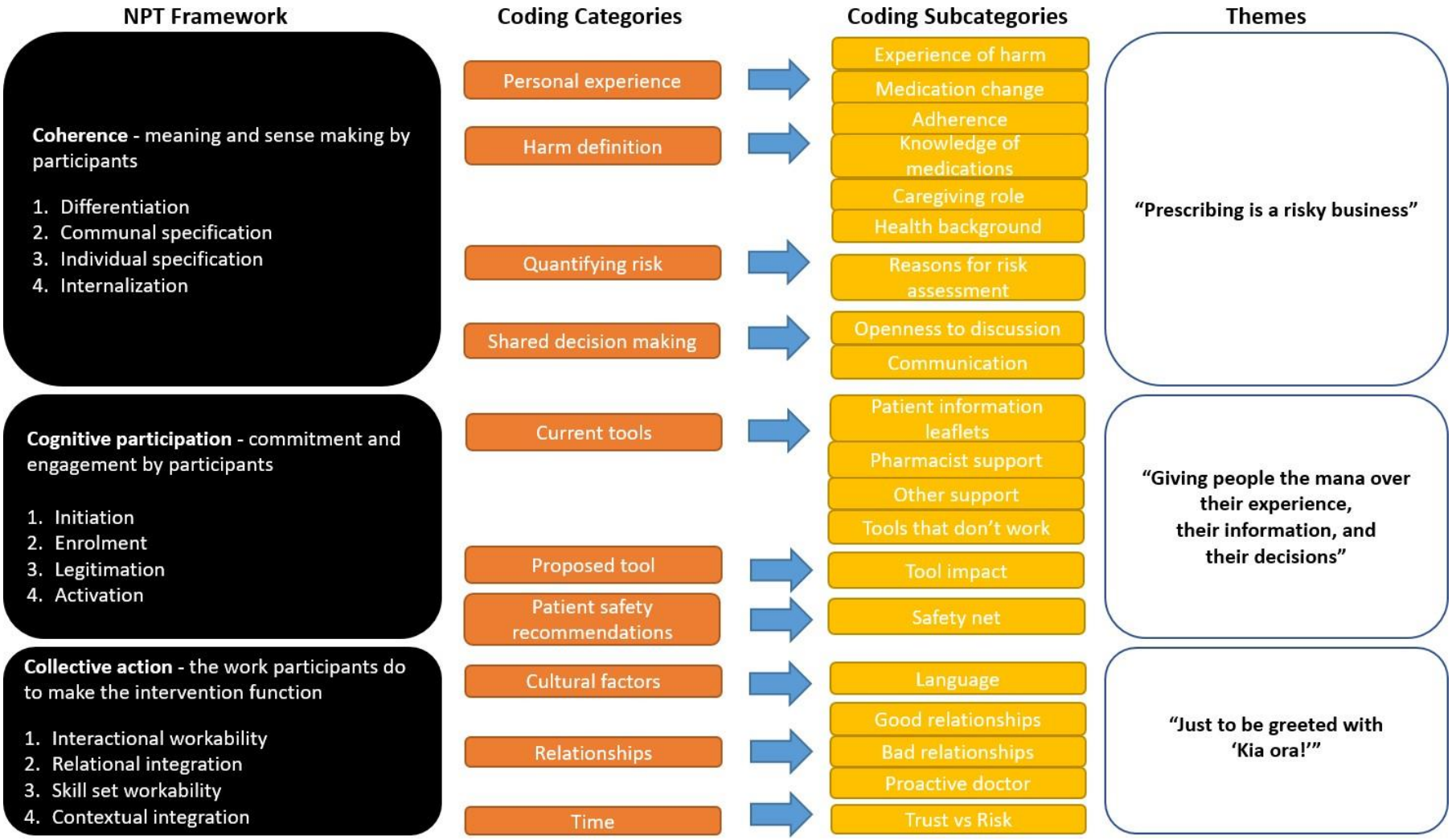

Figure 4-1 Relationship between NPT framework, coding categories and themes

4.7.1. Theme 1 – "Prescribing is a risky business" [Coherence]

Recognising the tension between the risks and benefits of medication was critical for understanding the rationale for the project, and both doctors and patients expressed cognisance of this, drawing on their experience of medication harm. Doctors based their understanding of risks and benefits on their clinical experience:

> "*Medications are always a balance of gain or whatever you're trying to treat balanced against risks of potential side effects.*" Doctor 9 (European female)

Patients, on the other hand, referenced their personal or whānau (family) experiences:

> "*With the preventer I take, you do have a chance of getting oral thrush in your mouth. So that has happened to me a couple of times. Yeah. And it's a pain in the butt, but it's better than having an asthma attack so I knew that it might happen. And when it did, I was like, well, this is the trade-off. I prefer not to have an asthma attack.*" Patient 1 (Māori female)

> "*I think the more medication you take the more risk of things interacting. I mean, some of the things I take, it says if your kidney function's going down don't give it, and I think, I'm already on it. They know I'm on it. And, you know, I accept that there are just risks you've got to take.*" Patient 6 (European female)

The doctors reported tailoring the amount and type of information to share with their patients depending on their perception as to what the patient would like to know. Doctors relied on their knowledge of their patients to determine what level of shared decision-making was attempted:

"*I make a rough assessment depending on how well I know them, I suppose, about how much they understand. It's a dynamic thing with all those things as I go through thinking about it and discussing what we do, depending on how they respond, I can go a little bit differently. It's not a static thing.*" Doctor 7 (European male)

Doctors found communicating information about medication and medication risks difficult. Barriers to communication reported included time, the challenge of presenting information at an appropriate health literacy level, and a perception that some patients are not interested in this information. Doctors typically focused on communicating the important risks:

"*It takes a long time to explain small risks of harms so I tend to filter out the important ones, or the ones I feel are important.*" Doctor 3 (European male)

"*Our perception of risk is always very different to theirs. And also trying to communicate percentages, or you know, numbers needed to treat, all those sorts of concepts are very difficult for people to take on board.*" Doctor 9 (European female)

"*Health literacy is a real skill I think in connecting with people and communicating on their level... you don't always get that right. So it's as much for the aggressive, in a rush person who is frustrated at waiting thirty minutes and just wants to pick their pills up and get out of there, as much as it is for the person who can't read and write, and has difficulty in conceptualising how medications work, and what we mean by risk*." Doctor 5 (European male)

In contrast, patient participants were keen to have as much knowledge about their

medications as possible. Patients frequently wanted more information than their doctor or pharmacist provided. They were happy to find their own information, but were concerned about the quality of the information they found on the internet:

> "*I have admit that after five years I've only got a vague idea what my drugs actually do... I want to be more informed as to what my medication is…. I would like to be more empowered. To know what it is I'm taking and why I'm taking it*." Patient 2 (Māori male)

> "*You can research a lot, but authenticating what's genuine and what isn't as well can also be huge.*" Patient 9 (Māori female)

4.7.2. Theme 2 - "Giving people the mana over their experience, their information and their decisions" [Cognitive Participation]

The idea of the proposed tool was met with qualified enthusiasm from both patients and clinicians. Patients and clinicians wanted to include various elements as part of a risk assessment and communication tool (Table 4-3). Participants, both doctors and patients, were cautiously optimistic that the proposed tool would be beneficial. Doctors felt the tool had potential to reduce their workload, as having tailored risk information readily accessible could save time and be a useful resource for both patients and clinicians.

Conversely, they were frank to admit they would reject anything perceived to impact negatively on their workflow or on the doctor-patient relationship. Doctors thought that if the tool worked well, it could actually prevent medication related harm, reducing patient morbidity and pressure on the health system:

"*I guess you'd hope the hospital presentations would be lessened because of it, given the number of hospital admissions that are related to medication harm.*" Doctor 3 (European female)

"*Realistically the consequences could be enormous if harm was prevented, and hospital admissions were saved*." Doctor 6 (European male)

Patients were more positive than doctors about the concept of the tool. Patients envisaged the tool would provide them with trustworthy medical information that they could access both during their general practice consult and also later, independently of their doctor. They felt this would facilitate information sharing and decision-making with whānau. Patients equated medical knowledge with improved understanding and control of their health:

"*I'm surprised that doesn't already exist... I think what is really important is giving people the mana or the authority over their experience and their information and their decisions. I think everything else stems from that*." Patient 1 (Māori female)

"*So in terms of that decision making, some sort of tool that would allow me to know what it was I was taking and why would be helpful… And I suppose this is a more difficult one, I suppose red flags in terms of there are things that you should be keeping an eye on with this medication.*" Patient 2 (Māori male)

Table 4-3 Summary of what participants want in a prescribing and communication tool

Doctors and patients want
• A trustworthy, endorsed tool • A user-friendly tool that is intuitive • The capacity to use on different platforms (mobile, desktop)
Doctors want
• A tool embedded within the patient management system • A tool that is fast • The capacity to turn on/turn off/ignore tool or parts of the tool • A simplified interactions checker (so prescriber doesn't need to check each medication individually) • A tool targeted to reduce polypharmacy • Age and renal function integrated into any calculations • Children's weight integrated into prescribing calculations (and printed on label) • Pregnancy or pregnancy risk factored into recommendations • Ethnicity (and earlier onset of disease) factored into risk weightings • A simple risk severity grading system (e.g. traffic light system) • Other risk assessment tools integrated within the one tool (e.g. CHA_2DS_2-VASc) • Patient access to empower shared decision-making • Streamlined monitoring for medications • An audit function to the tool • Alerts which are highly clinically relevant • Alternative medication suggestions (e.g. current first line agents based on updated prescribing or antimicrobial guidelines)
Patients want
• Access to the tool independent of their doctor • A tool that is culturally sensitive (and perhaps the potential to change language) • Something that is free to use and will help them understand their medications • "Just right" amount of information: not too much nor too little • Risk information presented simply (e.g. traffic light system)

However both doctors and patients were concerned there was potential for the tool to exacerbate harm. Too much information could put people off taking their medication or induce the nocebo effect:

> "*How in-depth do we need to go? There are so many side effects, and we can impose our expectations of what patients might experience*." Prescriber 6 (European male)

> "*It would be useful, but I think it could potentially scare someone off having a medication*." Patient 10 (Māori female)

> "*If there was some kind of unintentional bias in the way medicines were talked about and explained, you might end up, I don't know, with one of two options sounding much more attractive than the other… so I think there could be unintended consequences of not being neutral about it.*" Patient 1 (Māori female)

The form of the tool was debated by participants. Doctors mainly discussed access from their perspective, access directly integrated into their electronic health record system being heavily preferred over a separate add-on website. Most patients thought some kind of app or secure website, such as accessing information via their patient portal, would be most useful and provide independent patient access. (In NZ, patient portals currently allow patients variable access into their own general practice records, depending on what their practice has chosen. Access ranges from minimal – booking appointments online and checking blood results, to open notes - where patients can see all parts of their record). Older patients stated they would not be able to access information if it was a technology-based tool. This barrier was recognised by most participants:

"*Maybe just the people who are not good with technology might struggle quite a lot*."

Patient 8 (European female)

4.7.3. Theme 3 – "Just to be greeted with 'Kia ora!'" [Collective Action]

Collective Action is underpinned by the concept of relational integration, which explores the effect of the intervention on human relationships, especially the effects on power and trust.[236,247] Although relationships were not a particular focus of the interview questions, this theme was discussed in detail by all participants. They recognised that the action of establishing a relationship between patient and prescriber is required before any meaningful use of a prescribing tool or shared decision-making can take place.

Patients were asked what features would enhance the tool and its use for them. Use of Māori and Pacific languages was seen as important for enhancing engagement and understanding both within the tool and when communicating with the clinician. Whānau are important contributors to decision making, therefore opportunities for including whānau need to be incorporated into decision making processes when using the tool:

"*Just to be greeted with 'Kia ora!' Little things like that make a big difference, I think when engaging with a clinician*." Patient 4 (Māori male)

"*Some people don't understand English. But having that written in their own language and they read it and understand it… I know some seniors that depend on their children or grandchildren to tell them and describe how to take the medicine or when to take the medicine. So I reckon that is really important*." Patient 14 (Pasifika female)

"*I think it's just important to include whānau in decision making. That's really important,*

which I think is not just cultural, it just should be done anyway. A collaborative approach." Patient 4 (Māori male)

Patients wanted clinicians to use culturally safe practices and to acknowledge that people of different cultures may not feel comfortable attending general practice. The power imbalance between patients and clinicians was thought to be exacerbated by traditionally deferential attitudes towards clinicians, especially if they were of a different gender to the patient. These factors can obstruct discussions of medication risk and shared decision-making, particularly in the time-limited setting of a medical consultation:

"*I think there's lots of different cultural things about going to the doctor and Māori really feel a lot of whakamā* [shyness/embarrassment] *when talking about some stuff or depending on the doctor they get*." Patient 1 (Māori female)

"*Sometimes in a way embarrassed to talk to the doctor. Our culture is a respect. Yeah. It's a culture is a respect to talk to the doctor, especially the woman talk to the man, the doctor, man doctor*." Patient 13 (Pasifika female)

"*When, as a traditional Pasifika person, you're told, 'This is what's going to happen. You're going to get this. And I know, because I'm the doctor, and I'm telling you that this medication will help whatever, your lumbago or hypertension or whatever it is.' All you say as a traditional Pasifika person, 'Yes, doctor. Yes, yes.' As soon as you walk into that room, as soon as you walk through that door, the stethoscope or the persona of the person, or whatever they're wearing, takes away your right of questioning, of understanding.*" Patient 12 (Pasifika male)

Trust was acknowledged by both clinicians and patients as an important contributor to

shared decision-making. While patient-centered care encourages patients to play an active role in their healthcare, the traditional approach of relying on the doctor's opinion is still an important factor in decision making:

> "*They trust us as their doctors… I can spend a lot of time discussing the pros and cons and they end up saying, 'Well what would you do, what do you advise?'*" Prescriber 3 (European male)

> "*I tend to rely on my GP, I've got quite a high degree of trust for them to be able to manage that that risk for me*." Patient 2 (Māori male)

> "*We've got a really great relationship. So I feel that he has got my best interest in mind when he prescribes something to me*." Patient 10 (Māori female)

A tool that provided clinicians with tailored risk information and promoted communication of that information in a culturally safe and respectful way, could enhance the doctor-patient relationship by facilitating shared decision-making. One patient thought the tool could potentially redress some of the power imbalance:

> "*It might be a model that would shift to having to patients having more power, I suppose than, rather than traditional is going to the doctor because you've got a sore throat and you come out with a prescription… I always think it's good when people personally have more power over what they need for themselves*." Patient 5 (European female)

4.8. Discussion

This research was conducted to determine what participants think about a proposed electronic prescribing, decision-support and communication tool. Doctors and patients

prospectively evaluated a theoretical tool in order to refine the design. The main findings are broadly consistent with existing research.

In theme 1 (NPT = Coherence) patients and doctors understood the underlying premises of the proposed tool, particularly the tension between benefits and risks of prescribing. Few patient participants felt they had a good understanding of their medications, as has been found previously.[248,249] Patients were able to clearly describe examples of both poor and excellent risk communication. An important finding is that patients preferred full disclosure of medication risks in a manner that they can understand. In contrast, doctors felt they give an adequate amount of information about medication and risk, based on their personal assessment of their patients, which may well reflect their own biases and exacerbate inequity.[250] These findings are consistent with previous research exploring patients' and doctors' attitudes towards information sharing.[251-255] As has been found elsewhere, doctors in our study typically found it difficult to communicate risk.[256-258]

Participants actively evaluated the tool in theme 2 (NPT = Cognitive Participation), offering many suggestions as to how the tool could best suit their needs. Clinicians described existing ineffective or unworkable tools as models to avoid. They would accept a tool as proposed only if it was useful and was not perceived to cause additional work at the time of the initial clinical encounter, (although if properly implemented the tool has potential to reduce their workload through the prevention of harms requiring further clinical review). Their statements echoed the vast body of literature outlining failed e-tools and alert fatigue.[137,138,259,260] It is critical software developers ensure the benefits of using any tool outweigh the clinical disruption associated with its use.[129] Also consistent with existing research, patients want reputable medicines information that they can access on their own

terms and in their own time.[248,251,261,262] Patients and clinicians were concerned there was a potential for the tool to generate negative health outcomes mainly as a result of the nocebo effect[e]; extant literature demonstrates both that these concerns have been shared by others,[251] and the validity of both nocebo and placebo effects[f].[263,264] It is difficult to differentiate between a nocebo effect, and patients accurately identifying adverse effects they have been warned about. Concerns were also raised about technology being a barrier for some patients, which is a known problem.[265,266]

In theme 3 (NPT = Collective Action) Patients and doctors stressed the pre-eminence of establishing culturally safe relationships. Cultural safety is recognised as an independent requirement for achieving health equity.[186,267] Participants emphasised the importance of communication, particularly the use of Māori and Pacific languages to facilitate understanding both in clinical settings and in the proposed tool. This is congruent with known strategies to improve cross-cultural communication, such as clinician training and enhanced use of interpreter services[240,268] Trust remains a bedrock of the doctor-patient relationship; without shared power this approach does not promote shared decision-making.[269] Patients want to play an active part in decision-making about their health, while clinicians felt there was a wider range of patient responses – some patients have no interest in shared decision-making. The literature appears to support both perspectives.[252,270-272]

The fourth NPT concept of Reflexive Monitoring,[243] which ascertains the impact of a tool, was considered less relevant to this prospective evaluation of a potential tool. Patients and

[e] Nocebo effect – a negative treatment outcome that occurs because the patient believes the treatment will cause harm (Latin, nocebo = to harm)

[f] Placebo effect – a positive treatment outcome that occurs because the patient believes the treatment will be beneficial. (Latin, placebo = to please) In clinical trials "the placebo" refers to an inert medication used to test the efficacy of another medication. Placebo/nocebo effects can arise from any medical treatment.

GPs were asked to imagine the potential system-wide effects of the tool, as well as the intended and unintended consequences that might arise from its use. Participants found these questions difficult to answer, therefore there was little relevant data pertaining to this concept.

4.8.1. Strengths and limitations

This study successfully determined what participants think about a proposed risk assessment and communication tool, and interprets this through the lens of NPT. This prospective assessment of the tool will be used to refine the proposed tool to ensure it meets the requirements of prescriber and patient end-users. This study lays the groundwork for future analysis of the tool as it progresses through development and testing phases. Future analyses will be able to focus on more practical elements of NPT review. Ultimately, it is hoped that use of the proposed tool will support patient understanding of their risk of harm from medication, facilitate shared decision-making, and improve the quality of informed consent, while not increasing health inequity. This research was designed to inform the development of a risk assessment and communication tool in NZ, therefore the findings may not be generalisable beyond this scope.

Participants were all volunteers, and may not represent typical patients and doctors. Due to recruitment via Facebook, it is not known how many people chose not to participate. Patient participants were highly engaged in their healthcare; all patient participants wanted more information about their medications and participating in shared decision- making. Conversely, prescriber participants reported a far wider range of patient interest in active participation in their healthcare. Similarly, prescriber participants were those who were

interested in quality improvement and healthcare technology, and might not represent typical clinicians.

Satisfactory ethnic diversity was obtained for patients, however each ethnicity group is not comparable in terms of education and background; NZ European patients were mainly unemployed or students, Māori patients in this study were typically highly educated, while the Pasifika patients were predominantly immigrants to NZ who spoke English as a second language. Patients therefore were not fully representative of their ethnic group, and this may limit the extent to which their views and experiences reflect the full range of views and experiences within their ethnic group. For example, traditional deferential attitudes towards doctors were discussed by Pasifika participants, but these attitudes are not universal amongst Pasifika peoples, particularly younger people and those born in NZ. Ethnic diversity among doctors was not intentionally sought and was consequently limited. Of the nine doctors only two were Māori, and there were no Pasifika doctors.

NPT was used as a framework for developing the questions and as a sensitising device developing the codes and themes (Figure 4-1). NPT was useful in this context, however our research findings suggest the emphasis of this framework could be rearranged slightly to augment the construct of Coherence. Theme 1 strongly suggests personal or whānau experience is a critical factor in understanding medication harms for patients, and to a lesser degree for doctors. The lived experiences that participants bring to the sense-making work of establishing coherence is not explicitly recognised within the construct of Coherence as it is currently defined.

Participants were united in highlighting the primacy of relationships in the context of healthcare provision and use of any prescribing and communication tool. Relational

Integration is included within NPT construct of Collective Action, but is only ranked second of the four elements that make up this construct. In earlier iterations of NPT, Relational Integration and the other three elements now contributing to the construct of Collective Action formed the entire Normalisation Process model.[273] It may be that when implementation of a patient-facing intervention is planned using NPT, the area of relational integration requires more emphasis.

4.8.2. Implications

Given Aotearoa New Zealand's current high levels of inequity based on ethnicity and socioeconomic status, it is vital to consider and pre-emptively address the potential of any new intervention to worsen inequity.[36,274] In general terms, "upstream" actions that focus on equity from a health policy or systems perspective, such as improving access by reducing co-payments for healthcare, have a far greater impact on equity than "downstream" interventions, such as education of individuals, or the use of a tool like that proposed.[274,275] However co-designing interventions tailored for the needs of different groups can reduce barriers to receiving healthcare and has the potential to reduce inequities arising from use of technological interventions.[266,276] It is likely that a multidimensional approach is required to reduce health inequities, founded on culturally safe and trustworthy relationships.[277] Targeted strategies to increase technology use can go some way to bridge the digital divide, such as public provision of computers and internet access, while family and clinician support can encourage older patients to use technology.[261,266]

4.8.3. Conclusion

Patients and doctors provided different perspectives when evaluating a proposed risk

assessment and communication tool. Patient participants were keen to take an active part in their health and participate in shared decision making about their healthcare, whereas doctors described a wider range of interest in patient participation. NPT was a useful theoretical framework to conduct this evaluation and identify both requirements for the tool and features to avoid. This co-design research identified ideas for the proposed tool which had not been previously considered, such as providing patients with access to information about their medicines independently of their doctor. Overall patient and doctor participants supported the development of the proposed risk assessment and communication tool, but recognised successful use of the tool requires culturally safe and trustworthy doctor-patient relationships. Use of Māori and Pacific languages in the proposed tool may enhance engagement and understanding.

4.8.4. List of abbreviations

GP – General Practitioner

HRC – Health Research Council of New Zealand

NPT – Normalisation Process Theory

4.9. Declarations

4.9.1. Ethics Approval and Consent to Participate

This project was approved by the University of Otago human ethics committee (19/020), and reviewed by the Ngāi Tahu research consultation committee. All participants consented to participate in this research.

4.9.2. Consent for publication

Participants consented to the publication of their anonymised data.

4.9.3. Availability of supporting data

Supporting data (interview transcripts) are not available for review as they contain information which may identify participants. A summary of anonymised supporting data is available from the corresponding author on reasonable request.

4.9.4. Competing interests

There are no known competing interests.

4.9.5. Funding

This research was funded by the Health Research Council of New Zealand (HRC Clinical

Research Training Fellowship held by SL 18/031).

4.9.6. Authors' contributions

SL conceived and designed the study with input from TS, AS and SC, and is the guarantor. SL undertook the interviews and analysed the data with input from TS, AS and SC. SL drafted the manuscript. All authors read, provided critical review and approved the final manuscript.

4.9.7. Acknowledgements

We would like to thank all the participants in this research project.

4.9.8. Authors' information

Not applicable.

4.10. Chapter Summary

This chapter explored what patients and prescribers would like in a decision support and communication tool. Patients and general practitioners were interviewed about their views on the theoretical tool. Their responses were interpreted using an implementation science perspective, in the form of Normalisation Process Theory. Participants supported the concept of the tool overall, and made specific suggestions as to how it would be most useful for patients and clinicians. The results of this study were used to inform the development of a targeted patient information package on non-steroidal anti-inflammatory drugs (NSAIDs). This information package is discussed further in Chapter 5.

Chapter 5 Feasibility of using an information package to reduce patients' risk of renal damage

5.1. Preface

This work in this chapter was informed by the findings of the previous chapters. Medication prescribed in NZ general practice harms patients, at an incidence of 73.9 harms per 1000 patient-years (Chapter 2). Clinician alerts have potential to prevent harm, but rely on clinician action (Chapter 3). Patients want relevant information about their medication from a trusted source, but clinicians lack time to fully inform patients about their medication (Chapter 4). Therefore, we wanted to develop a solution that meets the needs of high risk patients and test whether it was feasible to use in a research setting. We chose to develop an information package for patients, which they can access independent of their clinician. It consists of a PDF document (Figure 5-2), and an online learning exercise (https://www.healthnavigator.org.nz/medicines/n/nsaids-learning-activity/). The information package is designed for patients at risk of renal damage from their medications. It warns patients who are taking an antihypertensive plus a diuretic against taking anti-inflammatories.

5.1.1. Chapter Aim

A full randomized controlled trial is planned post-PhD to test whether this information changes patients' self-reported behavior. This chapter aims to explore the feasibility of providing patients with a tailored information package, and to determine whether there are

any obstacles to successfully undertaking the full trial.

The following chapter contains two parts:

1. The feasibility trial protocol, which is presented as a published original manuscript titled "Using an Information Package to Reduce Patients' Risk of Renal Damage: Protocol for a Randomized Feasibility Trial." It was published in JMIR Research Protocols in 2021: *Leitch S, Smith A, Zeng J, Stokes T. Using an Information Package to Reduce Patients' Risk of Renal Damage: Protocol for a Randomized Feasibility Trial. JMIR Res Protoc. 2021;10(4):e29161. doi: 10.2196/29161.*

2. The feasibility trial results.

American spelling has been used throughout this chapter, to maintain consistency with the published article.

PART 1: Avoiding the "triple whammy": study protocol for a randomized feasibility trial to pilot the use of an information package to reduce patients' risk of renal damage.

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5.2 Abstract

5.2.1. Background

Non-steroidal anti-inflammatory drugs (NSAIDs) are a common cause of renal damage, especially when taken together with angiotensin-converting enzyme inhibitors (ACE-i) or angiotensin II receptor blockers (ARBs) plus a diuretic – a combination known as the "triple whammy." New Zealand patients are at high risk of the "triple whammy" because they can easily purchase NSAIDs without a prescription and in non-pharmacy retail settings (e.g., the

supermarket), there is no legal requirement to include patient information sheets with medication, and direct-to-consumer drug advertising is permitted. A patient information package has been developed for those at greatest risk of the "triple whammy," consisting of a printable PDF and an interactive online learning activity. This information package aims to inform patients about their elevated risk of harm from NSAIDS, and discourage use of NSAIDs. A randomized control trial was planned to assess the effect of the information package.

5.2.2. Objective

This study aims to pilot the trial procedures for recruiting patients, providing patient information online and to assess the acceptability of the patient information package.

5.2.3. Methods

A two-armed randomized feasibility trial will be undertaken in Northland, New Zealand. We will recruit 50 patients who are at least 18 years old from those who have signed up to receive email alerts through their general practice. Patients eligible for this study have been prescribed an ACE-i or ARB, plus a diuretic in the past 3 months. They will be randomly allocated to 2 study arms. The intervention arm will receive access to an information package plus usual care; the control arm will receive usual care alone. Online surveys will be used to assess NSAID knowledge and NSAID use at baseline and after two weeks for both arms. The intervention arm will also evaluate the information package in an additional survey based on Normalisation Process Theory (NPT) concepts. We will report the number and proportion of participants who are eligible and consent to participate in the trial. Response and drop-out rates will be reported for each trial arm.

The numbers of patients who interact with the education package will be reported together with the patient evaluation of it.

5.2.4. Results

Funding has been obtained from the Health Research Council of New Zealand (HRC 18-031). The University of Otago Human Research Ethics Committee (H21/016) has approved this trial. Consultation has been undertaken with The Ngāi Tahu research consultation committee. The trial commenced on 1 April 2021.

5.2.5. Conclusions

This feasibility trial will test the study processes prior to commencing a randomized controlled trial and will determine the acceptability of the patient information package. We anticipate this work will provide useful information for other researchers attempting similar work.

5.2.6. Trial Registration

ANZCTR (Australian New Zealand Clinical Trial Registry): ACTRN12621000574842

5.2.7. Keywords

“triple whammy”; medication safety; patient education; general practice; NSAID; digital intervention; primary care

5.3. Introduction

Non-steroidal anti-inflammatory drugs (NSAIDs) are a common cause of renal damage.[278] The risk of renal injury dramatically increases when NSAIDs are taken together with

angiotensin-converting enzyme inhibitors (ACE-i) or angiotensin II receptor blockers (ARBs) plus a diuretic[279] – this is known as the "triple whammy" combination. Despite this issue being well known and publicized heavily to prescribers in recent years, coprescribing of these medications is still common in New Zealand; 2017 data suggests more than 26,500 patients were prescribed these medications concurrently, with the majority of these patients aged over 65 years.[280,281]

While prescribers should be well aware of the dangers of combining NSAIDs with other medications that alter renal perfusion, patients may not be.[282-284] The true extent of simultaneous use of these medications is unknown. Nonprescription use of NSAIDs may be high in New Zealand. This is due to the easy availability of NSAIDs for patients to purchase without a prescription and in non-pharmacy retail settings (e.g., the supermarket), no legal requirement to include patient information sheets with medication, and direct-to-consumer drug advertising.[262] Given these issues, it is important to maximize the opportunities to advise patients about the potential risks of taking anti-inflammatories as part of the "triple whammy."

Existing information for patients is generic and not generally considered fit-for- purpose.[262] Tailoring medication information for patients may improve the quality and usefulness of information, as well as improve patient knowledge.[285,286] However, examples of personalized medication information are rare.[287] Most patients consider doctors to be their main source of health information. Patients want to be able to share that information with their whānau (family) as well as health professionals,[255,288] but doctors do not always provide patients with that information.[248,289] Doctors find communicating risk information difficult,[256,258] and communicating potential risks of NSAIDs may be incomplete.[290] Time, low health literacy

levels, and lack of patient interest have been suggested as additional barriers to communication.[288]

Providing information directly to patients may help address some of those issues; however, information must be provided at an appropriate health literacy level. New Zealanders typically have low levels of health literacy – over half of all adults surveyed had skills "insufficient to cope with the health literacy demands they typically face."[159] When the health literacy study results were broken down by ethnicity, 75-80% of Māori (the indigenous people of Aotearoa New Zealand) and 90% of Pasifika (people living in New Zealand who migrated from or have ancestry in the Pacific Islands), had low health literacy levels.[159] Health literacy has been identified as a cause of health disparities,[157] and decision support tools can help address deficits in health literacy.[158,291] Self-efficacy, a patient's belief in their ability to undertake and successfully complete a task, is another factor highly associated with optimal medication use.[292,293]

Most medication information for patients is in leaflet form, with patient information resources becoming increasingly available online. Patients search for high-quality, reputable information, but find it hard to judge the quality of the information they find online.[288] A few studies have examined novel modalities of delivering health information to patients, but there is room for further research to evaluate the efficacy of alternative media modalities.[294,295]

Conporto Health Event Detection & Mitigation (Conporto) is a software package that detects whether general practice patients are at risk of harm from their prescribed medications.[147] The current system operates in real-time to detect if there is a risk of harm from pre-specified conditions, for example, if methotrexate is prescribed without a co-

prescription for folic acid or if allopurinol is prescribed at a dose of >200mg/day to a patient with chronic renal insufficiency. Clinicians are informed of each alert and then decide whether to take action or inform patients. Conporto has developed the capacity to contact patients directly via text and email, with patient consent. This patient contact is triggered when a patient requests a prescription from their general practice, and is currently used to inform patients that their prescription is ready for collection. This function could also be used to provide patients with more information about their medications.

We have developed a printable information sheet and an online learning activity for patients. Patients, general practitioners, pharmacists, and a patient education provider have contributed to the development of these resources, which aim to inform patients about their elevated risk of harm from NSAIDs, and discourage them from using over-the-counter NSAIDs. A randomized controlled trial (RCT) was proposed to examine the effect of giving at-risk patients this information directly, without needing their health care practitioners to provide it. This trial aims to assess the impact of providing an information package about avoiding anti-inflammatory medicines to patients at risk of renal damage from the "triple whammy," in particular, the impact on anti-inflammatory knowledge and self-reported behavior. However, we have a number of concerns that we need to address before carrying out the full RCT.

First, it is unknown if our recruitment methods will be successful in enrolling a representative sample of the target population. Second, a low response rate of online surveys is a common concern. Having a better understanding of the survey response rate will help us determine the number of participants needed for the full trial. Third, while we

have developed the information package with some patient input, it has not been formally evaluated by patients. Fourth, we don't know whether the survey questions are appropriate to assess the impact of the intervention. Therefore, we plan to conduct this randomized feasibility trial to assess the feasibility of the intervention, pilot the recruitment methods and the use of surveys for assessing the impact of the intervention. The results of this feasibility trial will help refine our methods prior to commencing a definitive RCT.

5.4. Aims

The primary aim of this study is to assess the feasibility of conducting a RCT. The RCT will investigate the effect of providing a patient information package about NSAIDs to patients at increased risk of renal damage because of their medications. The feasibility trial will elucidate any issues which could impair our capacity to answer the aims of the full trial.

The feasibility trial aims to (1) pilot the procedures for recruiting patients and providing patient information online to assess the number of eligible participants and the recruitment rate, assess the characteristics of participants who are enrolling in the trial, identify any technical challenges for patients assessing information online, and assess the drop-out rate in each group; (2) assess the acceptability of the patient information package to assess if patients trust and understand the information provided and think it is relevant to them; and (3) pilot the use of the survey for assessing the effects of providing patients information about the risk of NSAIDS to obtain preliminary data of the survey responses to help sample size calculation in the full trial, assess the response rates of the surveys, and assess the suitability of survey questions to measure the impact of the intervention.

5.5. Method

This will be a two-armed randomized feasibility trial. The trial will be conducted according to the steps outlined in Figure 5-1.

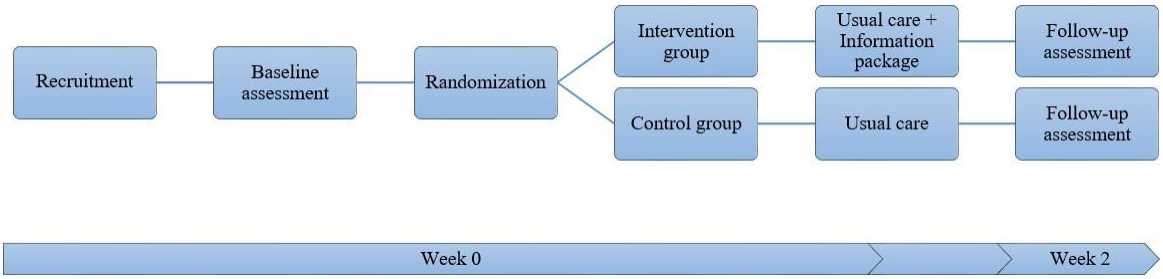

Figure 5-1 Flow chart of study protocol

5.5.1. Recruitment

Conporto is used by general practices across New Zealand. Patients attending general practices using Conporto in the Northland region will be eligible to participate in the randomized feasibility trial. Northland was chosen as Conporto is used widely in the region and it has a high proportion of Māori patients. Northland is a subtropical region in New Zealand, with a population of 179,000. Compared to the rest of New Zealand, Northland is more rural, is poorer, and has a higher proportion of people of Māori ethnicity.[296] Recruitment will be undertaken at the individual level. We aim to recruit 50 patients (25 patients in each trial arm), to pilot the use of the surveys. Participants will be allocated a unique study identification number to preserve anonymity.

Patients will be identified as having increased risk of harm from NSAIDs from their current prescriptions. Patients prescribed at least 2 of the 3 “triple whammy” medications (i.e., an ACE-i or ARB plus a diuretic) will be identified by Conporto. Patients will be eligible to

participate in this study if they were prescribed these medications concurrently in the past three months, are over 18 years old, and if they have signed up to receive Conporto's email messages. Box 5.1 describes participant inclusion and exclusion criteria. All eligible patients will be invited to participate in the study via email from Conporto.

Box 5.1: Participant eligibility criteria

Inclusion criteria

- Age 18 years or older
- Angiotensin-converting enzyme inhibitor (ACE-i) or angiotensin II receptor blockers (ARB) + diuretic in the past 3 months
- Signed up to receive Conporto alerts

Exclusion criteria

- Fails to complete enrollment

5.5.2. Randomization and blinding

Following recruitment to the study, patients will be automatically randomized 1:1 to either the control or intervention group within each practice. Patients will not be advised which group they are allocated to. Stata software will be used to generate the randomization sequence, which will be allocated using REDCap (Research Electronic Data Capture) software. REDCap software will also be used to administer all the surveys. REDCap is a secure web-based survey tool suitable for data requiring high security storage (i.e. patient data). Non-respondents at each stage will be emailed 2 further invitations to participate, at 1-day intervals.

5.5.3 Baseline assessment

The study invitation email will contain a link to the baseline assessment (Appendix 3). The first page of the assessment contains a consent form approved by the University of Otago

Human Ethics Committee. Once the consent form is completed, the rest of the form opens automatically to request demographic information, information about current medications and NSAID use, a validated single-item health literacy assessment,[297] a validated 4-item medicine use and self-efficacy questionnaire,[292] a validated NSAID knowledge assessment,[298] and a self-report of NSAID use in the preceding fortnight.

5.5.4 Study Intervention

Within 24 hours of completing the baseline assessment, intervention group patients will be emailed a link to a webpage containing a fully accessible, online, interactive learning activity and a downloadable PDF (Figure 5-2).[299] Patient information about avoiding anti-inflammatories and online interactive learning activity have been developed by SL in conjunction with the Health Navigator editorial board, their pharmacist, and the Health Navigator patient panel in an iterative process. The webpage is hosted by Health Navigator New Zealand, a non-profit initiative that provides curated health information overseen by the Health Navigator Charitable Trust. Both the control and the intervention group will receive usual general practice care from their own primary care team during the trial. After the trial is completed, control group patients will also be sent an email with a link to the information package, so all patients in the study eventually have access to that resource.

Avoid anti-inflammatories when taking blood pressure medicines*

*Except on the advice of your doctor

If you take ***these*** medicines:

Blood pressure pills

and

Water pills (diuretics)

Avoid taking ***these*** medicines:

Anti-inflammatories

Taken together these medicines can *seriously* harm your kidneys

Are you taking these?

Blood pressure pills

Cilazapril, Enalapril, Lisinopril, Perinodpril, Quinapril, Accuretic, Candesartan, Irbesartan, Losartan, Arrow-Losartan & Hydrochlorothiazide, Entresto

Water pills (diuretics)

Bendroflumethiazide (bendrofluazide), Chlortalidone, Indapamide, Metolazone, Furosemide, Bumetanide, Eplerenone, Spironolactone, Frumil, Moduretic

If yes, check with your doctor before taking these:

Common anti-inflammatories

Ibuprofen and combinations with ibuprofen	Brufen, Ibugesic, I-Profen, Nurofen, Advil, Medix, Nurofen Plus, Maxigesic, Nuromol, Brufen extra, Nurofen Cold and Flu
Naproxen	Noflam, Naprosyn SR, Naprogesic, Sonaflam
Diclofenac	Voltaren, Voltaren SR, Voltaren-D, Diclofenac (Dr Reddy's), Diclofenac Sandoz, Diclohexal, Apo-Diclo SR
Celecoxib	Celecoxib Pfizer, Celebrex, Celostea

Remember, if you are taking *blood pressure medicines*:

- Avoid anti-inflammatories if possible
- Ask your health provider before taking anti-inflammatories
- Only take one type of anti-inflammatory at a time
- Use the smallest dose of anti-inflammatories for the shortest time. Do not exceed the recommended dose.

Figure 5-2 Study intervention – information sheet

5.5.5 Follow-up assessment

All patients will be sent a follow-up survey after 2 weeks which repeats 2 survey items from the baseline assessment: the validated NSAID knowledge assessment[298] and the self- report of NSAID use in the preceding fortnight.

Patients in the intervention arm will also complete an additional survey (Appendix 3) to evaluate the information package. This evaluation survey is based on Normalisation Process Theory concepts (NPT).[242] NPT has been successfully used in the assessment and implementation of multiple patient-facing complex health interventions[236,237,300] and to evaluate other primary care initiatives aiming to reduce kidney injury.[301,302]

5.5.6. Measures

We will report the number and percentage of patients who are eligible to participate in the trial, and those who consent to participate. For participants in each of the study arms, we will report the response and drop-out rates for each of the surveys. The number of patients who open the information package will also be recorded via the website analytic data from the Health Navigator website. The numbers of patients who interact with the education package will be reported, together with the patient evaluation of it. NSAID knowledge scores and self-reports of NSAID use will be measured at baseline and 2-week follow-up.

5.5.7. Statistical analysis

Descriptive analyses will be carried out to summarize the characteristics of the participants in each study arm. Preliminary data will be obtained for the NSAID knowledge scores and self-reported NSAID use at baseline and follow-up to guide sample size calculation for the

full trial. If numbers allow, linear mixed models will be used to compare the changes in the mean score on the NSAID knowledge questionnaire and self- reported NSAID use between the 2 arms.

5.6. Results

Funding has been obtained from the Health Research Council of New Zealand (HRC 18- 031). The University of Otago Human Research Ethics Committee (H21/016) has approved this trial. Consultation has been undertaken with The Ngāi Tahu research consultation committee. The trial commenced on 1 April 2021.

The expected outcomes include that we will determine the uptake, acceptability, and self-reported effects of providing patients with information about the risk of NSAIDs via a webpage; determine the feasibility of conducting this research via online survey, and these data will be used to apply for further research funding; and publications and conference presentation about trial results

5.7. Discussion

This feasibility trial will help us determine whether it is practical to conduct a nationwide RCT. It will help refine the information package. Additionally, it may provide preliminary data to help understand whether providing information directly to patients increases their knowledge or changes their behavior.

5.7.1. Strengths and limitations

This trial will evaluate the entire implementation process, testing trial processes and the

acceptability of the intervention. The results of this feasibility trial will ensure best use of limited health research funding for any future similar studies. Publication of this work will help other researchers considering conducing similar patient-focused research.

Language, education, and technology can be barriers to health literacy.[229] The main limitation of this research is that patients with the greatest barriers to health literacy are likely to experience those same barriers in accessing the proposed intervention and participating in this research project. The research project and proposed intervention were developed only in English due to financial constraints. If this intervention is successful in English on full testing, it is hoped funding will be made available to translate the intervention into different languages (e.g. Māori, Samoan and Tongan in the first instance).

A potential risk of this work is that patients experience anxiety or distress when they realize they are at increased risk of harm from medication. This risk is mitigated by the ubiquitous nature of health information readily available to patients, and the repeated encouragement for participants to discuss their concerns with their healthcare providers.

5.7.2. Comparison with Prior Work

Only a handful of feasibility trial protocols have been published to date in the field of primary care medication safety. Feasibility studies focus on testing and evaluating the study processes to assess "can it work?", while pilot studies focus on outcomes to assess the effectiveness of the intervention, or "does the intervention show promise?"[303] Feasibility studies are particularly important for complex interventions, which risk of being undermined by problems that could be otherwise sorted at an exploratory stage, such as the target population failing to engage with the study or intervention.[304] Testing the feasibility of a

project improves the chance of success of a larger trial, thus ensuring better use of funding and reducing the risk of harms arising from the intervention or study processes.[304]

5.8. Conclusion

This feasibility trial protocol describes our plan to test trial processes prior to commencing a nationwide randomized control trial. It will provide important information about the acceptability of the patient information package. We anticipate this work will offer a useful model for other researchers attempting similar work.

5.8.1. Acknowledgements

We are grateful for Conporto's collaborative approach in agreeing to work together to improve patient health. Thanks to Health Navigator New Zealand who agreed to host the online content; special thanks to their editorial board, pharmacist and the volunteer patient panel who provided extensive feedback on the patient information package. Thanks also to Jacob Dollman-Low for designing the information sheet.

5.8.2. Authors' Contributions

SL developed the trial protocol and wrote the manuscript under the supervision of JZ, AS and TS. JZ provided critical review of the statistical methods, the trial protocol and this manuscript. AS and TS provided critical review of the trial protocol and this manuscript.

Figure 5-3 Should I take ibuprofen?

[g] Thanks to Andy Leitch for modelling for *JMIR Research Protocols* at short notice. Photo by Sharon Leitch.

PART 2: Randomized Feasibility Trial Results

The protocol was followed without any amendments. As planned, all eligible patients attending general practices using Conporto in the Northland region were invited to participate in the randomized feasibility trial – in total 177 patients were eligible to participate. The trial commenced on 1 April 2021. Data collection concluded on 6 May 2021.

5.9. Recruitment

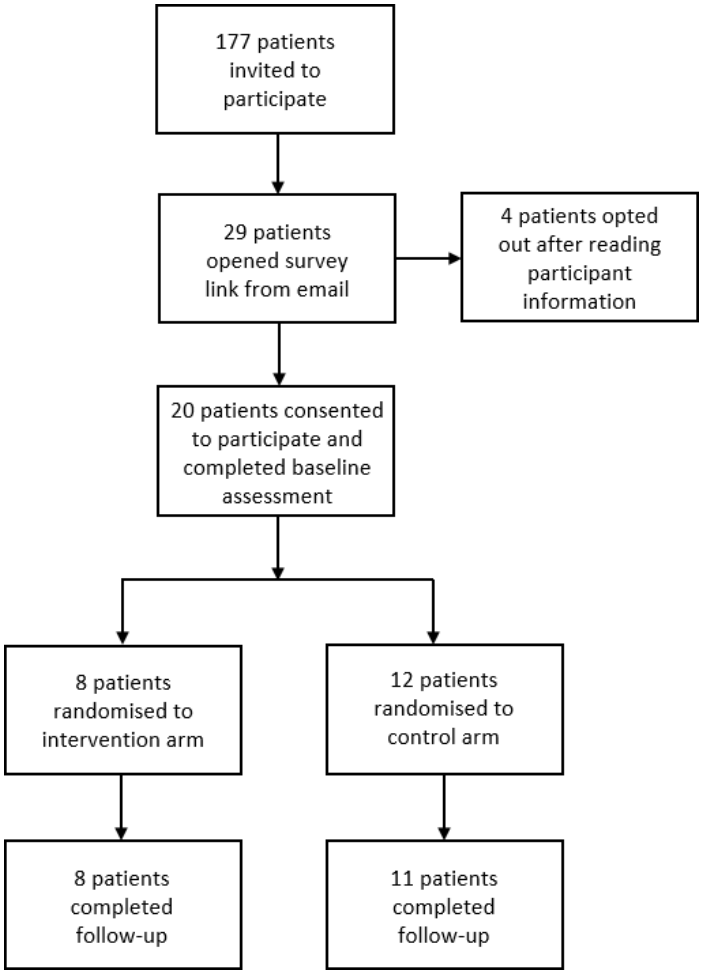

Figure 5-4 Recruitment and randomization flow-chart

The 177 Northland patients aged 18 years and older who met the eligibility criteria for the study were sent a total of three email invitations over the course of 10 days from Conporto. All 20 patients who consented to participate completed the baseline assessment and were randomized 1:1 into either the intervention group or the control group as per the protocol (Figure 5-4). The intervention group were emailed a link to the information package (https://www.healthnavigator.org.nz/medicines/n/nsaids-learning-activity/), and all patients were sent a follow-up assessment via email 14 days after completing the baseline assessment as planned. Participants were sent three reminder emails, at 24 hour intervals to complete the follow-up assessment. Only one participant did not complete the follow-up assessment, from the control group.

5.10. Variables

Anonymized demographic data for the eligible Northland population was extracted from the general practice records. Socioeconomic deprivation is calculated using geographical meshblock data of residential address (NZDep13)[195] and is automatically populated with the general practice data. Participant demographic details were self-recorded by participants, but meshblock data was not collected as it is based on residential address and collecting that data would have been a privacy issue. Instead, educational levels were recorded by participants as a coarse marker of socioeconomic deprivation and literacy. Ethnicity is self-reported in New Zealand; prioritized ethnicity was used.[174] Knowledge scores were assessed by summation of the total correct answers in the knowledge quiz, to give a score out of a maximum of 7 points.

Participants characteristics are reported with the mean and standard deviation (SD) for

continuous variables; the number and percentage are given for categorical variables by treatment arms. All analyses were performed in Stata 15.1.[196]

5.11. Results

Eleven percent of the eligible population were recruited to participate in this study (20/177), and nearly all participants completed the follow-up knowledge survey (19/20, 95.0%) (Figure 5-4). Potential participants were carefully screened prior to recruitment to ensure they were all eligible to participate based on their prescribed medications in the past three months. In spite of this, two patients' self-report of current medications did not include all the pre-requisite medication. We elected to include the data from those patients in the study results. Both patients were randomized to the control group.

Compared to the patients eligible to participate, the study patients were slightly older, with a higher proportion of females and less ethnic diversity (Table 5-1). Eligible patients tended to be from areas of high deprivation, with 57% in NZDep13 quintiles 4 and 5 (101/177). We were not able to obtain the addresses and therefore the NZDep13 results for the recruited patients, but instead requested their education level. Sixty percent of the study population had university education (12/20).

Table 5-1 Characteristics of eligible patients compared with recruited patients

	Eligible patients n=177	Recruited patients n=20
Age	65.7 (SD 11.8)	69.0 (SD 8.3)
Age range	29-94 years	54-89 years
Gender Female	89 (50.3)	13 (65.0)
Ethnicity		
NZ European	107 (60.4)	16 (80.0)
Māori	47 (26.6)	4 (20.0)
Pasifika	1 (0.6)	0
Asian	3 (1.7)	0
Other	19 (10.7)	0
NZDep13 (Missing n=5)		
1 (least deprived)	14 (8.2)	n/a*
2	22 (12.9)	n/a
3	29 (17.0)	n/a
4	48 (28.1)	n/a
5 (most deprived)	53 (31.0)	n/a
Education		
High school	n/a**	8 (40.0)
University	n/a	12 (60.0)

*NZDep13 information not collected for recruited patients

** Education levels unknown for eligible population

Table 5-2 compares the baseline characteristics of participants randomized to intervention and control groups. The two groups were roughly equivalent in terms of age, gender, ethnicity, and education. Health literacy and self-efficacy scores had a wider distribution, with lower scores in the intervention group than in the control group. There was a similar distribution of preferences of sources of medication information in each group between healthcare providers and online information.

Table 5-2 Comparison of baseline characteristics of participants randomized to intervention and control groups

	Intervention n=8	Control n=12
Age	66.6 years SD 7.6	70.6 years SD 8.7
Age range	54-77 years	59-89 years
Gender Female	6 (75.0)	7 (58.3)
Ethnicity		
NZ European	6 (75.0)	10 (83.3)
Māori	2 (25.0)	2 (16.7)
Education		
Highschool	3 (37.5)	5 (41.7)
University	5 (62.5)	7 (58.3)
Single Item Self-Literacy assessment [297]		
How often do you need to have someone help you when you read instructions, pamphlets, or other written material from your doctor or pharmacy?		
Never	5 (62.5)	11 (91.7)
Rarely	2 (25.0)	1 (8.3)
Sometimes	1 (12.5)	0
Medication Use and Self-Efficacy [292]		
It is easy for me to ask my doctor about my medicine		
Agree/strongly agree	8 (100)	12 (100)
Disagree/strongly disagree	0	0
It is easy for me to understand my doctors instructions for my medicine		
Agree/strongly agree	8 (100)	11 (91.7)
Disagree/strongly disagree	0	1 (8.3)
It is easy for me to understand instructions on medicine bottles		
Agree/strongly agree	7 (87.5)	12 (100)
Disagree/strongly disagree	1 (12.5)	0
It is easy for me to get all the information I need about my medicine		
Agree/strongly agree	7 (87.5)	11 (91.7)
Disagree/strongly disagree	1 (12.5)	1 (8.3)
Medication Information Preferences		
I prefer receiving medication from my doctor, pharmacist or other health provider		
Agree/strongly agree	7 (87.5)	11 (91.7)
Disagree/strongly disagree	1 (12.5)	1 (8.3)
I prefer finding information about my medicines online		
Agree/strongly agree	6 (75.0)	5 (41.7)
Disagree/strongly disagree	2 (25.0)	7 (58.3)

5.11.1 Information package evaluation

Only 50% (4/8) patients randomized to the intervention group reported reading the information sheet and completed the online learning module, but the information package evaluation was fully completed by at least six participants (6/8, 75.0%). One person

commented that they could not download the PDF, but no other technical issues were reported. All evaluations were included in the results.

Evaluation of the information package is outlined in Table 5-3. Scores could range from 0 (strongly agree) to 100 (strongly disagree), so scores less than 50 suggest agreement, and scores greater than 50 suggest disagreement. Participants generally agreed that they understood why they were sent the information about anti- inflammatory medicines (mean 31.9, SD 33.7), although question 1 had the most divergent scores.

The first evaluation question (*I understand why I was sent the information about anti-inflammatory medicines*) had the most divergent scores, however Questions 2 (*the information made me worried about my medicines*), 3 (*the information helped me learn about anti-inflammatory medicines*) and 4 (*the information made me aware of my risk from anti-inflammatory medicines*), yielded equivocal results, with scores around 50 (i.e., neither agree nor disagree). Participants generally felt the information didn't help facilitate communication with their healthcare provider or family/whānau (questions 5 and 6). They generally found the information sheet simple to understand; the learning module was easy and didn't take too long (questions 7-9). Participants found the online learning module was a more effective learning tool than the information sheet (question 10).

Table 5-3 Information package evaluation

Question	Mean (SD)*
1. I understand why I was sent the information about anti-inflammatory medicines (n=7)	31.9 (33.7) Range 0-98
2. The information made me worried about my medicines (n=7)	52.9 (28.9) Range 18-90
3. The information helped me learn about anti-inflammatory medicines (n=7)	50.7 (26.5) Range 17-77
4. The information made me aware of my risk from anti-inflammatory medicines (n=7)	45.4 (23.8) Range 14-88
5. The information helped me to talk to my healthcare provider about my medicines (n=7)	54.7 (25.7) Range 27-90
6. The information helped me talk to my family/whānau about my medicines (n=7)	64.7 (15.1) Range 50-87
7. The printable information sheet was confusing (n=7)	64.4 (15.5) Range 46-88
8. The online learning module was difficult (n=7)	56 (10.3) Range 50-72
9. The online learning module took too long (n=7)	58.6 (12.4) Range 50-81
10. The online module helped me learn more than the information sheet (n=6)	42.0 (12.5) Range 23-50

*Scores could range from 0 (strongly agree) to 100 (strongly disagree)

5.11.2. Preliminary results – knowledge scores and self-reported action

Knowledge scores remained relatively static for both groups (Table 5-4). Around one quarter of patients reported NSAID use in the preceding fortnight at both baseline and follow-up, and all users obtained their NSAIDs with a prescription from their healthcare provider. NSAID use frequency ranged from “less than once a week” to “every day”. Around a third of participants at baseline and follow up intended to take action after completing the survey, such as to talk to their healthcare provider or to reduce/stop NSAIDs.

Table 5-4 NSAID knowledge, use, and self-reported action

	Intervention n=8 baseline & follow-up	**Control n=12 baseline (11 follow-up)**
NSAID knowledge		
Baseline	mean 4.3 (SD 0.8) range 3-5	mean 4.0 (SD 0.4) range 3-5
Follow-up	mean 4.3 (SD 0.5) range 4-5	mean 4.5 (SD 1.4) range 3-7
NSAID use in the past fortnight = yes		
Baseline use	2 (25.0%)	3 (25.0%)
Follow-up	2 (25.0)	3 (27.3)
Self-reported action = yes		
Talk to healthcare provider		
Baseline	1 (12.5)	1 (9.1)
Follow-up	2 (25.0)	1 (9.1)
Reduce/stop NSAIDS		
Baseline	2 (25.0)	2 (18.2)
Follow-up	1 (12.5)	1 (9.1)
Continue NSAIDS		
Baseline	0	1 (9.1)
Follow-up	0	2 (18.2)
None of the above		
Baseline	5 (62.5)	8 (72.7)
Follow-up	5 (62.5)	7 (63.6)

5.12. Discussion

This feasibility study demonstrated that email from a known provider of health information was a successful recruitment method. Eleven percent of eligible patients were recruited. Recruited participants had a higher proportion of females than the eligible population, were less culturally diverse, and probably were less socio- economically deprived based on the high proportion with university education. 60% of the study population had a university education, compared to only 9.6% of people living in Northland (2018 Census).[296] Retention between baseline and follow-up assessments was excellent, with only one person dropping out of the study. However, half of the patients randomized to receive the information

package reported they did not engage with the material.

The survey was successfully piloted; participants were able to complete the survey questions, and the survey questions were understandable and suitable for measuring patient knowledge. The effect of the intervention appears to be small, but these figures will be used to conduct the sample size calculation for the full trial.

5.12.1. Strengths and Limitations

Eleven percent of eligible patients were recruited for this study. This recruitment rate is similar to what Conporto has observed in other email campaigns,[305] but it is far higher than in recent published literature for studies using patient portal and email messaging. One study recruiting patients at risk of falls only had an enrolment rate of 0.17%,[306] a study looking at healthy lifestyle and body weight had an enrolment rate of 2.9%,[307] while a gout study reported a response rate of 4% to patient portal messaging.[308] We worked with Conporto Health to contact eligible patients by email. Patients attended practices that used Conporto Health services, and had already consented to receive other health- related information via email from the same service, some activated by the patient using their patient portal. (For example, a patient requesting a repeat prescription via their patient portal would receive an automatically generated email from Conporto Health once the e-prescription had been sent to their pharmacy.) It is likely patient familiarity and trust of Conporto Health emails led to higher recruitment rates than observed in the literature.

We anticipated that this study might not recruit patients with low health literacy who would potentially most benefit from the intervention.[309] This was confirmed with substantial differences between study participants and the eligible population in terms of

gender, ethnicity, and socio-economic deprivation. People with lower health literacy levels may struggle to understand informed consent documents, resulting in anxiety and reluctance to participate in clinical trials.[310] People with lower education levels and those who are more socioeconomically deprived are less likely to use technology to access health information, while women and younger people are more likely to do so.[266,311] This is consistent with the participant demographics in this study. Recruitment of a representative cohort may require the use of a variety of methods to reach under-represented groups.[308] However, recruitment of an unrepresentative sample will not affect the results of the full randomized controlled trial.

The information package was developed in conjunction with a patient panel and health-providers, but we also wanted research participants to complete a formal evaluation of the package. Only 7 participants completed the information package evaluation. We are unable to complete the formal evaluation of the information package as planned in the study protocol.[309] Usability studies assess design factors that affect the user experience of operating and navigating an application for an intended purpose.[312] In usability studies of technological interventions, a sample group of approximately 5-20 patients may be considered sufficient to evaluate the intervention.[313-315] Other feasibility and pilot studies testing e-health technologies associated with medication have had similar low numbers. One medication information pilot study had only 11 participants,[316] one study looking at medication information in the elderly had 16 participants,[317] and one usability and feasibility study aiming to reduce unsafe medication use had only 17 patients.[315] In retrospect, it would have been beneficial to get all participants to evaluate the information package, not just the intervention arm. In the full trial, participants will also be asked to

evaluate the information package as that data is lacking in our current understanding of the tool.

5.12.2. Comparison with the Literature

eHealth interventions, such as this information package, are cheap to develop and deliver, and are an easily scalable method of informing targeted patients about their medications. Printed material, software and other eHealth technologies have been effective in promoting health education in the community, among patients of all ages.[318,319] Knowledge and skill acquisition from multimedia education is superior to usual care (ad hoc education provided as part of normal clinical care) and no education.[318] Online programmes have been successful in medication education, promoting decision-making and supporting patient self-efficacy.[319,320] Education interventions that target over-the-counter medications have also improved safe medication use and medication self-efficacy scores.[320,321] Other similar studies that have also informed patients directly (rather than via their clinicians) have been successful in promoting shared-decision making and making safer medication choices.[322,323]

Our preliminary results suggest that our information package will be similarly beneficial, although a full trial is needed to fully evaluate the learning potential of this intervention. It is unknown whether providing this information package will promote patient discussion with healthcare providers, improve shared-decision making about medications, or reduce use of NSAIDs in high-risk patients. However, as discussed in Chapter 4, patients want access to high-quality medical information independent of their healthcare providers.[288] Targeting patients rather than healthcare providers is an underutilized and under-

researched method for promoting medication safety.[315,324] Coordinating educational campaigns for patients and clinicians may increase the efficacy of both.[315]

5.12.3. Conclusion

This randomized feasibility trial demonstrated that this research method is feasible for the purposes of recruiting patients and testing the effects of providing this targeted information package. Preliminary findings suggest the patients most likely to benefit from the intervention are less likely to participate in this type of research. A full randomized controlled trial is planned to formally test the effects of the targeted information package. Should the full trial demonstrate the information package is useful, further research will be needed to determine how to best disseminate it to patients at greatest risk.

5.13. Chapter Summary

This chapter describes the protocol and results from a randomized feasibility trial exploring the workability of providing patients with a targeted information package. The methods of recruitment and information provision were feasible. The impact of providing the information package needs to be fully tested in a randomized controlled trial, which is to be conducted after the conclusion of this PhD.

Chapter 6 Discussion

6.1. Preface

This chapter provides a summary of the whole thesis and a discussion of the salient points. The chapter commences with a discussion of the complexity of medication-related harm, seeing it as a "wicked problem." The major results from each of the four studies are presented, followed by a general discussion of the strengths and limitations of the methods used in this thesis. Three main issues are compared with the literature. Firstly, the importance of the patient perspective is highlighted in defining harm and developing solutions. Second, consideration is given to applying a systems perspective to improving patient safety. Finally, the inevitability of patient harm is debated. The contribution of this thesis to patient safety literature is discussed. The implications of this work, together with unanswered research questions, are outlined.

6.2. Introduction

Medication-related harm is a complex problem. Simple problems can be clearly defined and are relatively easy to solve, such as mathematics and chess problems. In contrast, complex problems are ill-defined and lack obvious solutions. Medication-related harm is a complex problem which could be regarded as a "wicked problem."[325] Box 6-1 describes the key characteristics of a wicked problem.

Box 6-1 Characteristics of a wicked problem[325]

1. Wicked problems are hard to define
2. It is hard to know when the problem is solved
3. Solutions are judged by interests and values; there are no correct solutions
4. The solutions cannot be tested easily
5. Every attempt to solve the problem is important
6. It is not possible to describe all potential solutions
7. Each problem is essentially unique
8. Each problem can be considered a symptom of another problem
9. Explanation of discrepancies determines the way the problem will be resolved
10. The problem solver has no right to be wrong

Medication-related harm has all the above characteristics:

1. Defining medication-related harm is difficult, as lamented by patient safety experts and discussed further below.
2. It is impossible to know how much medication-related harm has been averted through any one solution.
3. Solutions are not value-free. Success depends on how the intervention or harm is valued, which in turn depends on the societal or individual context. For example, low NZ immunisation rates were partly attributed to culturally dissonant

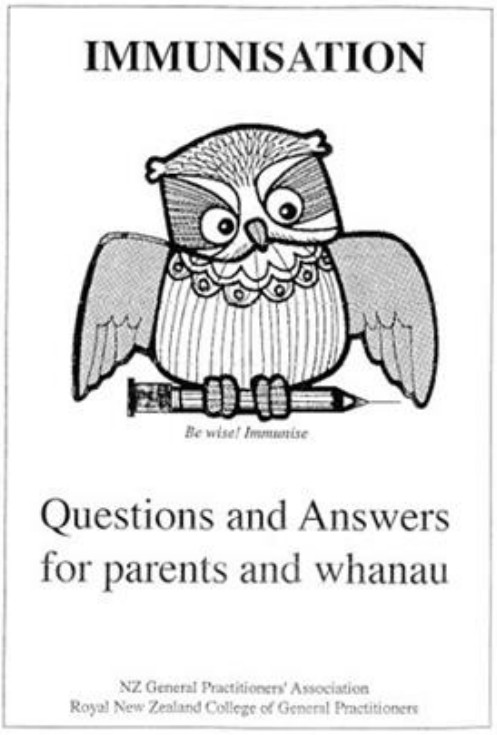

Figure 6-1. Immunisation material developed without Māori consultation

imaging in promotional material – the wise old owl of European lore is a harbinger of death in Māori legends (Figure 6-1).

4. Solutions can be tested, but there are many variable factors in each test which are difficult to take into account.
5. Getting it wrong even once can have serious consequences for a patient and their whānau.
6. There are innumerable potential solutions to the problem of medication-related harm.
7. Patients have individual risk-profiles, which vary through their life-course and in different states of health.
8. One problem leads to another. For example, a patient with angina is prescribed regular aspirin to prevent a myocardial infarction. This causes a little gastrointestinal bleeding. They also experience increased indigestion, so are prescribed omeprazole, which reduces B12 absorption. The patient gradually becomes anaemic resulting in blood tests, iron and B12 therapy, and potentially a colonoscopy or gastroscopy. Each investigation and treatment carries risk of additional harm.
9. Explanation of discrepancies determines the way the problem will be resolved. If a medication-related harm is defined in terms of prescriber error, the solution will be to provide prescribers with more education. If it is attributed to the medication, this may result in restriction in use of that medication. Alternatively, it may result in public outcry calling for systems change, as evidenced by the public response to six deaths potentially caused by a change in the brand of the anti-epileptic medication lamotrigine available in New Zealand.[326]
10. The problem solver has no right to be wrong. Medical culture contributes to unrealistic expectations of perfection and infallibility.[327] Compulsory medical indemnity

insurance suggests NZ patients and society expect health care providers to be right – if not all the time, at least most of the time.[328] Until the Crimes Act was amended in 1997, New Zealand clinicians could be held criminally liable if their patient died as a result of even minor acts of negligence. (The amendment brought NZ law in line with other similar countries. Now criminal law is applied only if the clinician's actions are judged a major departure from a normal standard of care.[329])

The "wicked problem" of medication-related harm can seem insurmountable, but is worth grappling with.[330] People seek medical care when they need help. Harming patients when they seek health care is morally wrong, costly, and detrimental to patients and clinicians alike.[31,331] "*The harm to patients resulting from medical errors at the most vulnerable moments of their lives is a profoundly intimate experience for everyone involved. Clinicians and staff are also deeply affected when they are involved in an adverse event and frequently suffer shame, guilt, fear, and long-lasting depression*."[332] Reducing harm from medication use in general practice is an important and worthwhile goal that requires creative thinking, adequate funding and sustained effort to achieve.

This thesis aimed to identify problems associated with medication use and then to explore strategies to improve medication safety in New Zealand general practice. Four studies were undertaken to address those aims. The first two studies identified factors that are associated with problems with medication use, by analysing data from two general practice record review studies. Study 1 estimated the incidence of medication-related harm in New Zealand general practice using data from the Safety, Harms and Risk Reduction Project (SHARP) (Chapter 2). Study 2 explored whether clinician action differs across ethnicity groups using

data from the Conporto Health proof-of-concept study (Chapter 3). The second half of the thesis considered strategies to improve medication safety. Interviews with patients and prescribers in Study 3 investigated what they would like from a medication decision support and communication tool (Chapter 4). Study 4 used knowledge gained from the preceding three studies to develop a tailored information package on avoiding NSAIDs for patients at risk of renal damage (Chapter 5). It further evaluated the feasibility of conducting a randomised controlled trial to assess potential benefits of the information package in improving knowledge of NSAIDs and reducing self-reported NSAID use in patients at risk of renal damage.

6.3. Summary of principal findings

6.3.1. Study 1: Medication-related harm arising from prescribing in NZ general practice

Data from a large retrospective review of general practice records (from 2011-2013 inclusive) were analysed to identify and describe the incidence of medication-related harm arising from prescribing in New Zealand general practice. The incidence rate of all medication-related harms was 73.9 harms per 1000 patient-years; for preventable or potentially preventable medication-related harms the incidence was 15.6 per 1000 patient-years. The majority of harms were minor (1390/1762, 78.9%), but one in five harms were moderate or severe (373/1762, 21.2%); three patients died. Eighteen study patients were hospitalised, equating to a hospitalisation rate of 1.1 per 1000 patient- years. Greater age, number of consultations, and number of medications were associated with higher risk of medication-related harm. Cardiovascular medications, antineoplastic and immunomodulatory agents, and anticoagulants caused most harm by frequency and

severity.

6.3.2. Study 2: Evaluation of equity in use of an automated clinician alert system

An automated GP alert system was found to be effective in reducing the risk of patient harm, but concerns were raised about whether there were ethnic inequities in steps taken to mitigate harm. The persistence of significant health disparities experienced by Māori and Pasifika is extensively documented. Data from a retrospective review of alerts and the corresponding general practice patient records were evaluated to see whether Māori and Pasifika patients were more or less likely to have action taken. No difference was found in the odds of having action taken among ethnic groups after adjusting for potential confounders, however, the estimated odds for Māori and Pasifika patients having action taken were lower than for European patients (Māori OR 0.88, 95%CI 0.63-1.22; Pasifika OR 0.88, 95%CI 0.52-1.49). Females had significantly lower odds than males of having action taken (OR 0.76, 95%CI 0.59-0.96).

6.3.3. Study 3: Patient and prescriber perspectives on a decision support and communication tool

An extended decision support system was proposed to both alert clinicians and patients about elevated risk situations. Patients and GPs were interviewed about this proposed tool to see what their priorities and preferences were. Patients want as much information as possible about their medications and risk, but doctors find it difficult to communicate that information to their patients. Participants were cautiously optimistic about a prescribing decision support tool, but worried about potential harm arising from its use. Participants identified requirements for the tool and features to avoid. For example, both doctors and

patients wanted a reputable tool that had been formally endorsed, that was intuitive to use and available on different platforms; conversely a tool that was slow, expensive or difficult to use should be avoided. The success of any patient safety tool is dependent on culturally safe and trustworthy doctor-patient relationships.

6.3.4. Study 4: A feasibility trial of an information package to reduce patients' risk of renal damage

Improving the quality of patient medication information is crucial to improve patient understanding about their medications and any greater risk from those medications. A feasibility study was undertaken to determine the practicality of the study processes, with a focus on evaluating recruitment strategies, acceptability and suitability of the intervention. The targeted population were patients at greater risk of renal damage from non-steroidal anti-inflammatory drugs (NSAIDs). The intervention was an information package advising them of that risk. Recruitment was by email to patients attending clinics using the Conporto Health alert system. I77 eligible patients were identified from the dataset and were invited to participate in the feasibility trial. Eleven percent of the eligible population agreed to participate (20/177), and most participants completed the follow-up survey (19/20, 95.0%). Participants reported few technical issues accessing the information package and found it simple to understand. The online learning module was regarded a more effective learning tool than the information sheet. NSAID knowledge scores remained relatively static, but approximately one third of participants reported they intended to discuss their NSAID use with their healthcare provider. This feasibility trial demonstrated patients are willing to participate in a study via email recruitment, and engage with an interactive learning activity online. The effect of the intervention appears to be small, but the results obtained in this

feasibility trial will be used to conduct the sample size calculation for the full trial.

6.4. Strengths and limitations of the chosen methods

Laboratory data, clinical trials, and trigger tools provide quantitative data for orderly analysis, but fail to account for the daily chaos of busy general practice clinics in their communities.[333] A strength of this thesis is that much of the work is based on real-world data. Real-world data are derived from multiple sources, such as claims data and electronic health records, and can be linked for more in-depth analysis.[334] Using these data for research purposes offers potential for cost-effective and timely research into medication use, quality and safety, and they are routinely used for post-market adverse event monitoring.[335-337] Routinely collected data were pragmatically used in this thesis to investigate medication safety in New Zealand general practice; Study 1 used data collected for the purposes of providing patient care, while Study 2 used data collected by a commercial organisation (Conporto Health) for their proof-of-concept trial.

The record review method, as used in Studies 1 and 2, is the gold standard method of patient safety research.[51] The main limitation of this method is that harms may go undocumented, as the content of medical records is mostly determined by the clinician entering the data. In addition, record reviewers struggle to agree on the presence of harm, harm preventability and severity, as evidenced by low-to-moderate inter-rater reliability scores across the literature.[51] More consistent data recording in electronic health records is required before these data could be routinely used for medication safety research and healthcare quality improvement.[338,339]

Trigger tools are used to expedite systematic and standardised record review studies.[43]

Future refinement of trigger tools and improved coding practices (e.g., using the Systematised Nomenclature of Medicine Clinical Terminology, SNOMED CT) may provide an acceptable standard for detecting and monitoring known harms.[51,340] Companies like Conporto Health use a trigger tool approach to automatically screen electronic records and prospectively alert clinicians to patients at higher risk of harm. Using data obtained with this type of technology for research is an obvious next step, and was demonstrated in Study 2.

One of the overriding themes of this work has been a lack of shared definition for patient safety terms. Despite a substantial body of work aiming to classify and define these terms over the past two decades, there remains a multiplicity of definitions, hindering patient safety research.[23,24,26,176,341] Similarly, our capacity to compare findings from different studies and examine the precision of harm estimates is hindered by a lack of agreed definitions for harm, harm severity, and harm preventability.[342] Medication error, adverse drug event, critical incident and never-event describe an event but not the outcome. Only some events result in patient harm. This thesis has focused on patient harm.

Medication-related harm was regarded from the patient perspective, a recommended approach which is discussed in the section below. However, one of the contentious elements of considering harm from a patient perspective was the inclusion of financial costs and opportunity costs associated with medication-related harm. It is hard to find these elements of harm discussed in patient safety literature, but they are a major problem for patients. Thirty-four percent of New Zealanders aged 15-44 years report the most common barriers to seeking medical help to be GP appointment cost and the cost of taking time off work. [343]

Stakeholder engagement in health care, research, policy and governance marks an important transition from traditional paternalistic care to personalised patient-centered

medicine.[245,344] Patient engagement is recognised as having a wide range of beneficial outcomes, including improved health literacy, clinical decision making, self-care and self-management, and patient safety.[345] Valuing the opinion of all stakeholders - patients as well as clinicians - led to the interviews conducted in Study 3. Data from those interviews contributed to the material developed in Study 4.

One of the main limitations of pursuing technical interventions, even low-tech interventions such as information provision in Study 4, is that the people who would most benefit from the intervention are often unable to access it due to technological barriers, low English literacy, and low health literacy. Older patients interviewed in Study 3 did not typically use technology such as computers or smart phones, preferring paper-based resources. Our intervention contained a printable information sheet, but it requires motivation, hardware, and a small amount of technical knowledge to print it off. Stakeholders also recommended developing the resources in different languages, especially Pasifika languages. We lacked the resources to undertake the necessary translation and consultation work. This is an area for future attention.

6.5. Comparison with the literature

6.5.1. Patient harm – collateral damage of healthcare in a complex system?

Patient harm may be considered an inevitable consequence of humans administering advanced socio-technical interventions in a highly complex system to people who are often physiologically compromised, and who are sometimes desperately unwell.[346] Indeed, many patient safety terms are qualified by the concept of "acceptable minimum" harm.[347]

"*Patient safety is the absence of preventable harm to a patient during the process of*

healthcare and reduction of risk of unnecessary harm associated with healthcare to an acceptable minimum. An acceptable minimum refers to the collective notions of given current knowledge, resources available and the context in which care was delivered weighed against the risk of non-treatment or other treatment. Therefore, it is the minimum prerequisite for high-quality care."[348] This approach is consistent with the risk management concept of keeping risk "as low as reasonably practicable" or ALARP, and "so far as is reasonably practicable" or SFAIRP.[349]

These pragmatic considerations must be kept in balance with the sometimes devastating effects of medication-related harm. Writing off the trauma of a medication-related harm as some kind of "acceptable" collateral damage in the provision of healthcare is likely to be unpalatable to patients and families who have experienced severe harm. Accepting a narrative of inevitable patient harm is defeatist and demotivating for efforts to understand and improve medication safety.[330] In Study 1 the majority of medication-related harms were deemed not preventable; importantly, about one in five harms was judged potentially preventable or preventable. These potentially preventable harms are where we must concentrate our attention and energy. Further research on the SHARP dataset is planned to explore the nature of the medication-related harms considered preventable or potentially preventable, and determine whether there are any particular demographic characteristics associated with a greater risk of experiencing those harms. Preventable patient harm is caused by multiple factors, but predominantly by health systems and clinicians working within those systems.[30,330] A systems approach is likely to provide the best opportunity to identify targets for in order to effect meaningful change.[129]

6.5.2. Patient perspective

Just as patient-centered health care is considered an essential domain of health quality,[350,351] including the patient perspective is an important element in patient safety research.[352,351] Ignoring stakeholders can result in developing inappropriate or harmful interventions, as in the immunisation owl example at the start of this chapter. Māori consultation radically altered the immunisation promotional material presented earlier (Figure 6-1), as seen in Figure 6-2. The new poster depicts the three baskets of knowledge (which the god Tāne stole from the heavens to help mankind), and a rainbow (representing power from the gods). Māori immunisation rates still lag other ethnicities, but have improved over time.[353,354] Similarly, building from a shared understanding with patients of the problems and potential solutions for medication-related harm increases the likelihood of success for each intervention.

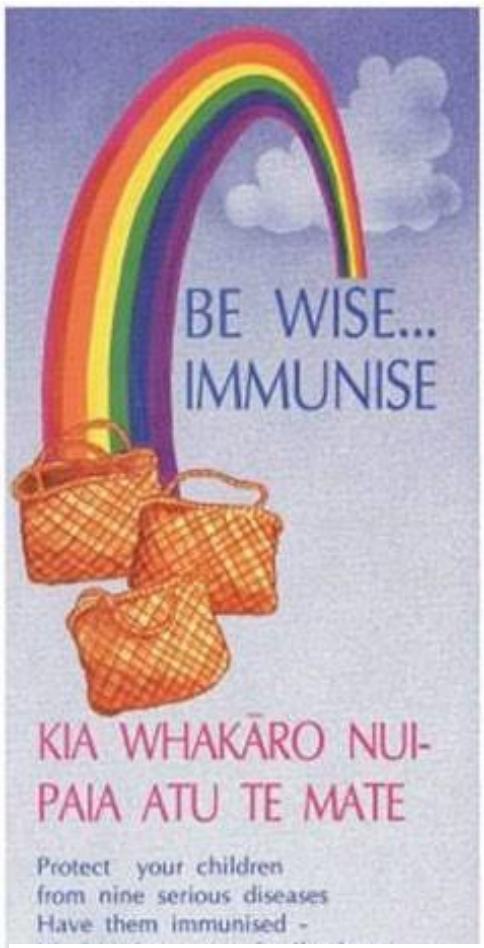

Figure 6-2 Immunisation poster developed with Māori consultation

Considering health care safety from the patient perspective has been recommended as a key method of promoting transformational change of the health system.[332,355] Best practices for patient involvement have not yet been established, but encouraging and empowering patients or their family members to speak up if something doesn't seem right is one strategy widely recommended to improve medication safety.[115,245,332,356]. Improved patient

access to medical advice is another method of improving patient safety. Increasing use of patient portals, email, telephone and video consultations are already improving healthcare accessibility, and may help reduce or mitigate medication-related harm.[357,358] Patients and clinicians have been willing to explore the use of mobile apps for reporting medication risk and providing advice in research settings.[340,359] Key recommendations for patient involvement are summarised in Box 6-2.

Box 6-2 Summary of key recommendations from Safety is Personal: partnering with patients and families for the safest care[332]

Target group	**Recommendation**
Policy makers	• Involve patients in policy-making • Use safety metrics that foster accountability and transparency • Engage patients in setting and implementing the research agenda
Health system leaders	• Involve patients and families in organisational activities • Train staff to be effective partners with patients and families • Partner with patient advocacy groups and organisations to increase public awareness and engagement
Clinicians and staff	• Provide patients and families with the information, training and tools they need to manage their health • Engage patients as equal partners in safety improvements • Support patients and families when things go wrong
Patients, families, the public	• Ask questions about care, understand medicines and care plans • Repeat back instructions and information to clinicians • Bring a friend/family member to appointments • Understand who is in charge of their care

The first two groups, policy makers and health system leaders, have the capacity to influence patient safety from a systems perspective. This thesis has focused on the last two groups in

Box 6-2 – clinicians and patients. As per WHO recommendations, it has tried to "*empower patients, families and their carers to become actively involved and engaged in treatment or care decisions, ask questions, spot errors and effectively manage their medications*," by putting "*mechanisms in place, including the use of tools and technologies, to enhance patient awareness and knowledge about medicines and medication use process, and patients' role in managing their own medications safely*."[115]

6.5.3. Systems perspective to improve patient safety

A systems approach to patient safety underpins the work of this thesis. The concepts of human factors/ergonomics (HFE) and the Systems Engineering Initiative for Patient Safety (SEIPS) model were introduced in Chapter 1. Implementation science is related to systems theory, but is particularly concerned with the best method to embed evidence-based practice into routine care.[130] Normalisation Process Theory (NPT) is one such theory, which was used in Study 3 to prospectively evaluate a proposed risk assessment and decision support tool. NPT can help researchers anticipate implementation issues while developing a complex intervention and its evaluation.[235-237,242] Healthcare tools, such as decision support or alert systems, will only work if they are embedded into and do not impede workflow, as was reiterated by healthcare providers in Study 3.

Of course the scope for a systems perspective approach extends far beyond the implementation of an information package, (such as that proposed in Study 4). Systems thinking considers multiple facets of a problem, including cultural pressures, the law, organisational factors, individual behaviour, physical ergonomics and physical devices.[123,124]

A systems approach to reduce the harm from consumption of over-the-counter (OTC)

medications[h] can be illustrated in the following examples of access to OTC Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and paracetamol. As discussed in Study 4, use of NSAIDs can be harmful for patients at risk of renal damage due to their other medications. Paracetamol access has been debated recently in New Zealand, following a student's accidental death from paracetamol overdose.[360,361] A HFE approach can help understand the drivers which influence individuals choosing to purchase and consume OTC analgesia such as NSAIDs and paracetamol, as described below.

Current societal pressures indirectly encourage use of analgesia by valuing wellness and pain avoidance. Capitalist economies reward the "productivity" associated with employment (although largely ignore unpaid work[362]), therefore, being well enough to work is vital. Employees may feel pressure to attend work even when unwell.[363] Our society is built around the concepts of comfort and convenience – pain and suffering are seen as adverse events which should be prevented or alleviated.[364,365] The law determines that small-volume packets of paracetamol and ibuprofen tablets are general sales medicines – they are available for purchase in pharmacies and other retail outlets. Larger packs and different formulations of these medications are available as pharmacy-only medicines or restricted medicines.[366] Individual behaviour is the other factor which is most likely to determine whether a person will take OTC medications or not. Addressing these factors to reduce OTC medication use is a complex exercise. Some economists have attempted to change the way society values work.[362] Encouraging safe work practices and culture may address

[h] OTC medications are available for purchase by the public without a prescription. They are classified into three main groups by availability:

- Restricted medicines (pharmacist-only medicines - available for purchase only after speaking to apharmacist)
- Pharmacy-only medicines (can only be sold in pharmacies)
- General sales medicines (available from pharmacies and other retail outlets)

presenteeism. Health professionals are some of the worst culprits in attending work while sick; targeted professional development programmes may help clinicians both recognise when they are unwell and give themselves permission to take time off.[363] Perhaps a simpler approach is to amend the law to further restrict the availability of these medications. However, such action may result in inadvertent harm, such as increased cost due to administration of compliance measures at a pharmacy, or inequity if people are unable to purchase these medications without a prescription, resulting in needless suffering.

In short, healthcare systems are deeply complex. Addressing healthcare safety within the context of a healthcare system goes well beyond the application of any one simple check-list or tool, but instead requires understanding of the daily compromises that are made between healthcare safety and efficiency.[121,367] NZ lacks a systems approach to medication use and safety.[368] Examples include inequitable use of antibiotics, failure to prescribe anti-gout medications for those who need it, and poor access to medication due to cost.[368] Cultural misalignment means Māori patients seldom achieve medicines optimisation.[368,369] Working within the existing health system is necessary, but sometimes the system is so dysfunctional that a complete overhaul is considered necessary.

6.5.4. New Zealand health system reforms

A major review was undertaken to ascertain the state of the NZ health and disability system during 2018-2020.[190] The review found the system was overly complex and fragmented. It articulated a host of unsatisfactory outcomes, particularly in relation to existing health inequities for Māori, Pasifika, people with more socio-economic deprivation, people with disabilities, and people living in rural towns.[190] It found the health system has failed to

honour the Treaty of Waitangi by not supporting self-governance and self-determination for Māori healthcare.[368]

As a result, the NZ government announced major restructuring of the health system in April 2021.[370] The 20 district health boards responsible for funding and providing healthcare in each region will be replaced with a single agency, Health NZ. A Māori Health Authority will be established to ensure health policy and strategy supports Māori health, and the Māori Health Authority will commission Health NZ for healthcare services for Māori communities. The changes aim to reduce complexity and strengthen primary care. The proposed changes address major issues discussed in this thesis, including the need for improved equity, explicit partnership with Māori, person and whānau-centered care (where people have control over the management of their own health), and provision of continuously improving high-quality care.[370]

New Zealand is familiar with health system change; sequential major restructuring over the past four decades has been disruptive and expensive, with little benefit perceived at the healthcare coal-face.[187,371,372] Whether the proposed restructuring of the health and disability system achieves its laudable aims remains to be seen. Whatever the outcome, patient safety within the system remains of paramount importance.

6.6. Contribution to the literature

Each of the four studies described in this thesis has contributed to the patient safety corpus.

Study 1 assessed medication harm arising from prescribing in New Zealand general practice, as observed in general practice records. The Safety, Harms and Risk Reduction Project (SHARP) is the largest general practice record review study undertaken in New Zealand to

date. This study builds on the evidence base about the risk posed by medication in the real world. Findings can be used to inform decision-making in general practice and to target patient safety initiatives towards patients at higher risk of harm.

Study 2 re-evaluated data from an automated alert system to see if there were differences in clinician action depending on the ethnicity of the patient. Despite the importance New Zealand places on equity, there appears to be scant literature evaluating health care interventions and tools by ethnicity. This work has added to the body of knowledge on this topic and provides unique insight into New Zealand practice.

Study 3 prospectively evaluated a proposed risk assessment and communication tool by interviewing patients and clinicians using Normalisation Process Theory (NPT). The work considered the themes of safe prescribing, medical autonomy and cultural safety in the setting of New Zealand general practice. This work is useful for researchers developing tools intended for use by patients and clinicians, particularly in NZ and similar societies.

Study 4 explored whether providing patients directly with targeted medicines information via an email and internet was feasible. Few randomised feasibility trial protocols have been published, therefore this publication should assist other researchers planning their own feasibility studies. Our preliminary results found this method of targeting patients rather than clinicians for information provision was feasible.

6.7. Implications for approaches to patient safety and future research

This thesis has addressed medication safety in New Zealand general practice. Implications arising from this study may be considered in the following categories; health systems and health leadership, clinicians and healthcare staff, and patients and whānau, as broadly

described in Box 6-2 above.

6.7.1. Health systems and health leadership

The health system reforms present an opportunity to address medication safety from a national perspective. Centralisation of health funding and commissioning, together with standardisation of the health information technology used nationwide, should enhance the country's capacity to routinely audit and continuously improve medication safety.

Further research is required to corroborate the extent of harm arising from general practice as found in Study 1. It is not feasible to use extensive record review studies for routine safety monitoring, but this work provides a baseline epidemiology of harm which could be used to set audit parameters and ongoing priorities for medication safety research in New Zealand general practice.

Enhanced connectivity and compatibility of eHealth records,[190] should improve medication reconciliation and knowledge of patient alerts during patient transfers between care settings. More specific actions to improve patient safety could be also taken, such as a national roll-out of targeted alerts, (e.g., Conporto Health EDM, which resulted in clinician action in Study 2), or requiring prescribing software to prevent inadvertent concurrent prescribing of contraindicated medication (such as the "triple whammy").

The establishment of the Māori Health Authority presents a novel opportunity for health policy and health service commissioning to be influenced with a clear equity and partnership mandate. Study 2 found evidence of inequity in clinician action by ethnicity and gender; the Māori Health Authority could advocate for increased cultural safety and bias recognition training for health care workers. As discussed by patients and clinicians in Study 3, improved

access to healthcare and medications could help address New Zealand's high levels of inequity based on ethnicity and socioeconomic deprivation, and improving public access to technology could improve patient access to health information. This thesis has attempted to consider and pre-emptively address the potential of a new intervention to worsen inequity. Health equity requires repeated evaluation to measure the impact of health interventions and ensure new interventions are designed to reduce, or at least not exacerbate, existing inequities. It is within the Māori Health Authority's remit to advocate for further research in this area.

6.7.2. Clinicians and healthcare staff

Clinicians are extremely motivated to provide high-quality patient care.[327,328] Study 2 found targeted alert systems can help general practitioners dealing with increasing patient complexity by identifying patients at greatest risk of experiencing medication-related harm, and take mitigating actions to reduce the risk of patient harm. Clinicians could request wider use of such a system, which has the potential to reduce medication- related harm in general practice.

Addressing clinician biases may improve the equitability of health care provision,[267] as discussed in Studies 2 and 3. Clinicians are already required to do regular cultural safety training as part of their maintenance of professional standards activities. Specifically training clinicians to recognise their own biases and speak up against racism and sexism may help reduce inequities based on those characteristics.[267] Further research is required to determine whether this type of training reduces health inequities. Patient and clinician perspectives are required to develop workable solutions to the pervasive problem of medication-related harm.

6.7.3. Patients and whānau

Patient empowerment is an important strategy recommended to improve medication safety.[332,345] Improving access to medical information can help inform patients and their whānau, and improve their capacity to engage in dialogue about treatment options and advocate for themselves and their families in healthcare encounters.[318-320] Information packages, such as that tested in Study 4, are relatively simple to develop and cheap to deliver. Our study showed providing medication information directly to patients at risk of renal damage was feasible, but a full randomised controlled trial is required to determine whether this information package can change knowledge or behaviour. The information was provided in English only; another study could examine whether presenting information in Māori and Pasifika languages enhances engagement and understanding. Further testing of the information package will determine its effectiveness; if successful, then the method described in Study 4 is easily scalable.

6.8. Conclusion

This thesis builds on the evidence base about the risk posed by medication in the real world by examining aspects of medication-related harm in New Zealand general practice. Medication-related harm in general practice is common – but most harm is minor and not preventable. Clinicians typically take action on alerts arising from a general practice electronic alert system, but possibly take less action for women and Māori and Pasifika patients. Patients and doctors felt the most important aspect of healthcare is culturally safe and trustworthy doctor-patient relationships. Patients want to take an active part in their health; independent access to reliable information is a critical element in being able to participate in shared decision-making. This thesis has proposed a solution that may help

improve patient capacity in shared decision-making by delivering medication-risk information directly to patients. Further investigation will determine whether that information improves knowledge or changes behaviour. Solving the “wicked” problem of medication-related harm requires intentional health policy and leadership, unbiased clinician action, and inclusion of patient and clinical perspectives.

She asked me if she took one pill for her heart and one pill for her hips and one pill for her chest and one pill for her blood how come they would all know which part of her body they should go to.

I explained to her that active metabolites in each pharmaceutical would adopt a spatial configuration leading to an exact interface with receptor molecules on the cellular surfaces of the target structures involved.

She told me not to bullshit her.

I told her that each pill had a different shape and that each part of her body had a different shape and that her pills could only work when both these shapes could fit together.

She said I had no right to talk about the shape of her body.

I said that each pill was a key and that her body was a thousand locks.

She said she wasn't going to swallow that.

I told her that they worked by magic.

She asked me why I didn't say that in the first place.

Glenn Colquhoun[373]

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Appendix 1. COREQ checklist

Additional information for patient and prescriber perspectives on a decision support and communication tool, as per the consolidated criteria for reporting qualitative research (COREQ) checklist

Domain 1: Research Team and reflexivity	
Personal Characteristics 1. Interviewer/facilitator; 2. Credentials; 3. Occupation; 4. Gender; Experience and Training	SL conducted all the interviews. SL is a general practitioner with 12 years of clinical experience and 5 years of health research experience. This work was completed as part of her PhD, supervised by TS and AS. SC is a research advisor on this project. TS is an experienced researcher and general practitioner who has led and collaborated on externally funded (≈ NZ$7.8 million) health service delivery implementation research (UK & NZ) using both quantitative and qualitative methods. His research expertise in general practice and in quality improvement research is fundamental to this project. AS is an experienced investigator in the field of clinical pharmacy, focusing on quality use of medicines and Pharmacoepidemiology. She has experience developing and implementing trials of electronic decision support tools. SC is an experienced Māori health researcher and general practitioner. She helped plan the data collection, and provided cultural insights into the data analysis. All researchers were employed by the University of Otago. SL is a Clinical Research Training Fellow, TS is a Professor, AS is a Senior Research Fellow, and SC is an Associate Professor.
Relationship with participants 6. Relationships established; 7. Participant knowledge of the interviewer; 8. Interviewer characteristics	Collegial relationships were well established with the local Dunedin prescribers prior to the commencement of the study, who were personally invited to participate by SL. Invitation was made either face-to-face or via email. Several of the participants recruited via Facebook page “GPs for GPs” were also known to SL. Patients recruited for the study were unknown to SL. They were recruited via Facebook and Facebook Messenger, email or phone was used to arrange the

	interviews. SL was identified to all participants as a GP who was conducting research for her PhD research. SL has had extensive communication skills training through her undergraduate, postgraduate and vocational training. She has 18 years' experience working as a clinician, 12 years of those working as a GP.
Doman 2: study design	
Theoretical framework 9. Methodological orientation and theory;	The methodology of this paper is outlined in detail within the paper. It draws strongly on Implementation Science theory, particularly Normalisation Process Theory (NPT).
Participant selection 10. Sampling; 11. Method of approach; 12; Sample Size; 13. Non-Participation	A purposive sampling approach was taken for recruitment of both prescribers and patients. Initially Dunedin GPs were invited to participate in the study. This resulted in 5 face-to-face interviews with Dunedin-based prescribers. Subsequent prescribers were recruited on a closed Facebook page for New Zealand GPs, "GPs for GPs". Five people, four men and one woman expressed an interest in participating in the study, with the four men all participating in either phone or Zoom interviews. Patients of different ethnicities were sought for this project in an attempt to increase the diversity of the views. A Māori-owned company in Dunedin was approached for research participants, resulting in three interviews with Māori patients. Participants were then sought via a post on the "Dunedin News" Facebook page. This was an extremely effective method of recruitment, and a further two Māori patients, five NZ European patients, and one Pasifika patient were recruited. Pacific Trust Otago were then approached for recruitment. The Trust holds a weekly meeting for their elders, which includes exercise (provided by a physiotherapy student), food, a sing-along, and an occasional educational talk. SL gave an educational talk on medication safety at this meeting and recruited another four Pasifika patients. SL had no relationship with any patients prior to the study interview, apart from the Pacific Trust group as described. All participants received information about the study and signed a consent form approved by the University of Otago Human Ethics committee (19/020) prior to their

	interview. The study team anticipated that we would not need any more than 15 patient or GP interviews to reach data saturation in each group. SC suggested the ethnicity split 5 European/5 Māori/5 Pasifika as that would help us gain an understanding of the perspectives of different ethnicities. Due to recruitment via Facebook, it is not known how many people chose not to participate.
Setting 14. Setting of data collection; 15. Presence of non-participants; 16. Description of sample	Dunedin-based prescriber interviews occurred face-to-face, in either the prescriber's office, at the University of Otago, or in a café. All patients were Dunedin-based to allow face-to-face interviews. These took place in the patients' home, their workplace or at the University of Otago. Non-participants were not present during the interviews. Participants self-identified their personal characteristics, including age and ethnicity
Data collection 17. Interview guide; 18. Repeat interviews; 19. Audio/visual recording; 20. Field notes; 21. Duration; 22. Data saturation; 23. Transcripts returned	SL developed the interview guide following the NPT structure. This was reviewed by TS and AS, and refined through practice interviews. No repeat interviews occurred, but two prescriber participants sent additional material to SL via email following their interview. All but one of the interviews were recorded, due to a failure of the recording equipment on one occasion. Extensive field notes were taken during that interview and were written up immediately afterwards. Each interview lasted from 30-90 minutes. Interviews were either transcribed by SL or sent to rev.com for transcription, and all transcripts were closely reviewed and revised by SL to ensure they were as accurate as possible. Participants did not have the opportunity to review transcripts. Although the sample size was planned as executed, data saturation was observed within the last few interviews in each group, with no new ideas being discussed by participants.
Domain 3. Analysis and findings	
Data analysis 24. Number of data coders; 25. Description of the coding tree; Derivation of themes; 27. Software; 28. Participant checking	SL developed the coding structure and coded all data using NVIVO qualitative data management software.[374] Coding was reviewed in depth by TS. Codes were clustered into themes derived from the NPT framework and focussed on the development of the proposed tool.

	Participants were not involved at the data analysis stage.
Reporting 29. Quotations presented; 30. Data and findings consistent; 31. Clarity of major themes; 32. Clarity of minor themes	Quotations were extracted from the transcripts to illustrate the major and minor themes. These were checked during analysis to ensure they were not taken out of context of the interview, and consistently and accurately represented the participants' views.

Appendix 2. Interview Topic Guide

For patient and prescriber perspectives on a decision support and communication tool

Interview Topic Guide for Prescribers

Before we begin, do you have any further questions (about the consent process/study)?
Could you tell me a bit about yourself and your practice setting? How long have you been at this practice? How long have you worked as a GP (and in NZ if applicable)? Have you completed any extra qualifications on top of your medical degree? What is your list size? What is your role in the practice (partner/associate/locum)? What PMS does your practice use?
What prompts you to consider assessing a patient's risk from their medication? How do you currently assess patients' risk of medication harm? What tools do you use? Do you have support in this area from a pharmacist/secondary care?
How confident do you feel explaining medication risk to patients? What encourages/discourages you to discuss risk with patients? How open do you feel your patients are to discussing medication risk? When would you focus on medication risks and when would you focus on the benefits? Why? Do you use any resources to help explain concepts of risk to patients? What are they? Risk scenarios: *High risk patient*: elderly female, eGFR 20 mL/min, 10 long term medications, presents with increasing SOB likely due to deterioration of known congestive heart failure. *High risk medication*: Methotrexate/Insulin/Warfarin *High risk condition*: Psychosis/rheumatoid arthritis/cancer
What do you understand by the term shared decision making? How do you feel about shared decision making in your clinical practice? How do you promote shared decision making? How open do you feel your patients are to shared decision making? Have you ever had any training in promoting shared decision making with patients?
Can you describe a case (anonymously) where a patient has experienced problems from their medication that were potentially preventable? What stands out for you in this case that was different from other patients? What were the factors contributing to medication harm? What were the factors contributing to patient safety? You mentioned XXX as working well, do you think this could be supported in other cases? You mentioned XXX as working poorly, how do you think this could be changed?
Do you think the proposed MedKōrero tool, to assess risk and communicate that risk to patients, will promote shared decision making? What kind of impact would a tool like this have in your clinical setting? Would it be helpful to your day-to-day work? What would promote its use? What would be a barrier to its use?

What would be the top priorities for a patient safety tool like MedKōrero? High risk patients? High risk medications? High risk conditions?
Can you think of potential system-wide effects of using this tool? What would be the intended and unintended consequences
If you could make a recommendation/suggestion to improve patient safety in primary care in relation to medication use, what would it be? Explore patient factors in relation to these recommendations for larger implications
Can you think of anything else I should ask? Is there anything else I should ask other prescribers?

Interview Topic Guide for Patients

Before we begin, do you have any further questions (about the consent process/study)?
Could you tell me a bit about yourself and your experiences with medicine? How old are you? Ethnicity? Do you take medicine every day? When was the last time you were prescribed medicine? Do you help someone else regularly with their medication?
What does harm from medicine mean to you? What does risk from medicine harm mean? Can you give me an example? Synonyms of risk: danger, peril, possibility, hazard, menace, threat
When do you think it's important to know about your risk from medication? High-risk vs low-risk medications/conditions? Treatment vs prevention? Personal perception of risk (high risk patient)?
Do you think it's important to discuss medication risk with your GP? What encourages/discourages you to discuss risk with your GP? How open do you feel your GP is to discussing medication risk? When would you focus on medication risks and when would you focus on the benefits? Why? Have you ever been given information about medication risk? What was it? Was it helpful? Risk scenarios: *High risk patient*: elderly relative who is frail and on 10 long term medications. *High risk medication*: Methotrexate/Insulin/Warfarin *High risk condition*: Psychosis/rheumatoid arthritis/cancer
What do you understand by the term shared decision making? Can you recall a time when you felt like you and your doctor made treatment decisions about your health care together? How do you feel about shared decision making about your health care? How open do you feel your doctor is to shared decision making?
Can you describe a time when you or someone close to you experienced problems from their medication? What were the factors contributing to the medication harm? What were the factors contributing to patient safety?

You mentioned XXX as working well, do you think this could be supported for other people? You mentioned XXX as working poorly, how do you think this could be improved?
Do you think the proposed MedKōrero tool, to assess risk and improve communication about that risk, will help you/your whanau make decisions about treatment? Do you think it would promote shared decision making? What kind of impact would a tool like this have for you/your whanau when you are deciding on a treatment option? What would promote its use? What would be a barrier to its use?
What do you think should be the top priorities for a patient safety tool like MedKōrero? High risk patients? High risk medications? High risk conditions?
Can you think of potential system-wide effects of using this tool? What would be the intended and unintended consequences
If you could make a recommendation/suggestion to improve patient safety in primary care in relation to medication use, what would it be? Explore patient factors in relation to these recommendations for larger implications
Can you think of anything else I should ask you? Is there anything else I should ask other people?

Appendix 3. Baseline and follow-up surveys

For feasibility study using an information package to reduce patients' risk of renal damage

Baseline survey

Background information	
Age (years)	
Gender	○ Female ○ Male ○ Other ○ Prefer not to say
Which ethnic group do you belong to?	☐ New Zealand European ☐ Māori ☐ Samoan ☐ Cook Islands Māori ☐ Tongan ☐ Niuean ☐ Chinese ☐ Indian ☐ Other
Other Ethnicity	
Education **What is your highest level of education?**	○ No formal education ○ Primary school ○ Secondary school ○ University or Polytech
How often do you need to have someone help you when you read instructions, pamphlets, or other written material from your doctor or pharmacy?	○ Never ○ Rarely ○ Sometimes ○ Often ○ Always

Medication Self-Efficacy				
	strongly disagree	**disagree**	**agree**	**strongly agre**
It is easy for me to ask my doctor questions about my medicine	○	○	○	○
It is easy for me to understand my doctor's instructions for my medicine	○	○	○	○
It is easy for me to understand instruction on medicine bottles	○	○	○	○
It is easy for me to get all the information I need about my medicine	○	○	○	○

Medication

Have you taken any of the following medication in the past three months?

Do you take one of these blood pressure pills?

• Cilazapril • Enalapril • Lisinopril • Perindopril • Quinapril	• Candesartan • Irbesartan • Losartan • Entresto

○ Yes ○ No

reset

Do you take water pills (diuretics)?

Common water pills (diuretics):

• Bendroflumethiazide • Bendrofluazide • Furosemide • Frumil	• Chlortalidone • Metolazone • Bumetanide • Indapamide	• Eplerenone • Spironolactone • Moduretic

○ Yes ○ No

reset

Do you take one of these combined pills?

Combination blood pressure and water pills

- Accuretic
- Arrow-Losartan & Hydrochlorothiazide

○ Yes ○ No

reset

How do you prefer to learn about your medication?

	strongly agree	agree	disagree	strongly disagree
I prefer receiving medicine information from my doctor, pharmacist or other healthcare provider. * must provide value	○	○	○	○

reset

I prefer finding information about my medicines online * must provide value	○	○	○	○

reset

Baseline and follow-up surveys

Knowledge Quiz

Which of the following are nonsteroidal anti-inflammatory medicines?

Choose as many options as necessary

* must provide value

- ☐ Paracetamol
- ☐ Ibuprofen
- ☐ Pseudoephedrine
- ☐ Arthritis rubs (e.g. Deep Heat or Zostrix (capsaicin))

Do these conditions increase your risk of kidney disease?

	Yes	No
High blood pressure * must provide value	○	○ reset
Diabetes * must provide value	○	○ reset
Asthma * must provide value	○	○ reset

Anti-inflammatory medicines may not be safe to use in patients with kidney disease or at risk for kidney disease

* must provide value

- ○ True
- ○ False

reset

Taking anti-inflammatory medications can increase the risk of causing kidney damage

* must provide value

- ○ True
- ○ False

reset

If someone has high blood pressure or diabetes, what should they do if they need pain relief?

Choose as many options as necessary

* must provide value

- ☐ They should avoid anti-inflammatories even short term
- ☐ Anti-inflammatory medicines are not a problem in patients with high blood pressure or diabetes
- ☐ They should contact their pharmacist or other care provider before they consider using an anti-inflammatory medicine

Self-reported action

In the next month I plan to:

Choose as many of the following options as are relevant

- ☐ Talk to my doctor or pharmacist about my anti-inflammatory medicine use
- ☐ I plan to reduce or stop taking anti-inflammatory medicine
- ☐ I plan to continue taking anti-inflammatory medicine
- ☐ I plan to start taking anti-inflammatory medicine
- ☐ None of the above

Anti-inflammatory learning package evaluation

Anti-inflammatory learning package evaluation

Your feedback will help improve the information about anti-inflammatory medicine for other patients. Please complete the questions below.

The following questions relate to all the information you were sent about anti-inflammatory medicines.

I understand why I was sent the information about anti-inflammatory medicines

strongly agree — strongly disagree

* must provide value

Change the slider above to set a response

reset

The information made me worried about my medicines

strongly agree — strongly disagree

* must provide value

Change the slider above to set a response

reset

The information helped me learn about anti-inflammatory medicines

strongly agree — strongly disagree

* must provide value

Change the slider above to set a response

reset

The information made me aware of my risk from anti-inflammatory medicines

strongly agree — strongly disagree

* must provide value

Change the slider above to set a response

reset

The information helped me to talk to my healthcare provider about my medicines

strongly agree — strongly disagree

* must provide value

Change the slider above to set a response

reset

The information helped me talk to my family/whānau about my medicines

strongly agree — strongly disagree

* must provide value

Change the slider above to set a response

reset

Anti-inflammatory learning package evaluation: printable information sheet

The anti-inflammatory learning package was made up of two parts. The first part was the printable information sheet.

The following questions relate only to the printable information sheet.

Attachment: A4_Anti-Inflammatories_Final.pdf (0.2 MB)

I read the printable information sheet

○ Yes ○ No

* must provide value

reset

The printable information sheet was confusing

strongly agree — strongly disagree

* must provide value

Change the slider above to set a response

reset

Anti-inflammatory learning package evaluation: online learning module

The second part of the anti-inflammatory learning package was a link to an online learning module.

The following questions relate only to the online learning module.

Attachment: tab.JPG (0.04 MB)

I completed the online learning module

* must provide value

Yes No

reset

The online learning module was difficult

* must provide value

strongly agree strongly disagree

Change the slider above to set a response

reset

The online learning module took too long

* must provide value

strongly agree strongly disagree

Change the slider above to set a response

reset

The online module helped me learn more than the information sheet

* must provide value

strongly agree strongly disagree

Change the slider above to set a response

reset

How could we improve the information sheet or learning activity?

Expand